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SATURDAY OCTOBER 28 1950

TABLE OF CONTENTS

"Verities Yet in Their Chaos" CHARLES MCNEIL, M.D., F.R.C.P., F.R.C.P.Ed. 961

Anticoagulants in Treatment of Coronary Thrombosis
JOHN A. TULLOCH, M.D., M.R.C.P.Ed., and A. RAE GILCHRIST, M.D., F.R.C.P., F.R.C.P.Ed. 965

Capillary Resistance and Adrenocortical Activity
H. N. ROBSON, M.B., M.R.C.P.Ed., and J. J. R. DUTHIE, M.B., F.R.C.P.Ed. 971

Three Cases of Severe Burn Treated with Cortisone
P. O. CRASSWELLER, M.D., A. W. FARMER, M.D., W. R. FRANKS, M.D., and A. D. MCLACHLIN, M.D. 977

Unusual Complication of Myanesin Therapy in Treatment of Tetanus
M. L. NEWHOUSE, M.B., M.R.C.P., J. D. ROCHFORD, M.B., and G. RIDDELL ROYSTON, M.D., M.R.C.P. 981

Case of Tetanus Treated with Decamethonium Iodide R. MCD. S. KEIR, M.B. 984

Prolonged Intercostal Paralysis Due to a Relaxant H. BARRIE FAIRLEY, M.B. 986

MEDICAL MEMORANDA
Hypertrophy of the Little Finger. JAMES A. ROSS, M.D., F.R.C.S.Ed. 987
Status Epilepticus: A Symptom Complex of African Trypanosomiasis. EDWARD F. B. FORSTER, M.D. 987
Case of Double-headed Monster. S. D. KARVE, M.B. 988

REFRESHER COURSE
Migraine. MACDONALD CRITCHLEY, M.D., F.R.C.P. 996

GENERAL ARTICLES AND NEWS
PAEDIATRICS IN THE HARVEIAN AGE 997
BISSETT HAWKINS MEDAL 998
BIOLOGICAL ASPECTS OF ATOMIC ENERGY 999
SOCIETY OF MEDICAL OFFICERS OF HEALTH 1000
MEDICAL NOTES IN PARLIAMENT 1005
UNIVERSITIES AND COLLEGES 1009
MEDICAL NEWS 1011
BIRTHS, MARRIAGES, AND DEATHS 1013

QUESTIONS AND COMMENTS
Vaccination—Immunization and Poliomyelitis — Teething — The Vegetable Marrow—Vesical Calculus—Dangers of Detergents — "Gammexane" — Thrombophlebitis Migrans — Corrections 1013-14

Epidemiology Section 1010

LEADING ARTICLES
Anticoagulant Therapy of Acute Myocardial Infarction 991
Pay in the Salaried Services 992
Technique in B.C.G. Vaccination 993

ANNOTATIONS
Treatment of Tetanus 994
Smoking and Peptic Ulcer 994
Multiple Primary Neoplasms 995

REVIEWS
Weir Mitchell 989
The Breast 989
Venereal Diseases 989
Defective Children 990
Books Received 990

SUPPLEMENT
Glasgow Office of B.M.A. 175
PUBLIC HEALTH COMMITTEE 176
PUBLIC HEALTH SERVICE DEFENCE TRUST 176
PRIVATE PRACTICE COMMITTEE 176
OCCUPATIONAL HEALTH 177
Cost of Health Service in Scotland—WHITLEY COUNCIL REGIONAL APPEALS COMMITTEES—AMENDING ACTS COMMITTEE—PAYMENT ON ACCOUNT FOR EXPENSIVE PRESCRIPTIONS 177
QUESTIONS ANSWERED 178
CORRESPONDENCE 178
ASSOCIATION NOTICES 180

CORRESPONDENCE
Useless Routine Medical Examinations. THOMAS GIBSON, M.D. 1001
Child Health and the Future. I. GORDON, M.D.; CECILIA GALTON, M.R.C.S. 1001
Safety in Prams. JOAN MARSH 1002
Safety on Cycles. CHARLES S. THOMSON, M.B. 1002
Acute Liver Disease. J. M. WALSHE, M.B. 1002
Abnormalities in Developing Chickens. P. K. DURAISWAMI, F.R.C.S. 1002
Modification of Boyle's Apparatus. W. B. PRIMROSE, M.B.; J. MCN. INGLIS, M.B.; H. B. C. SANDIFORD, M.R.C.S. 1003
Treatment of Pink Disease. E. BRAUER, M.D. 1003
Observations on Cervical Erosion. DERK CRICHTON, M.B. 1003
Medical Students in Prague. J. ABELS, M.D. 1003
Smoking and Carcinoma of the Lung. LENNOX JOHNSTON, M.B. 1004
A Secret Remedy for Cancer. D. WRAGGE MORLEY 1004
Johann Mikulicz-Radecki. G. GREY TURNER, F.R.C.S. 1004
Male Toads Croak when Tickled. G. ENGLER, M.D. 1005
A Vestigial Tail. R. J. MCNEILL LOVE, F.R.C.S. 1005

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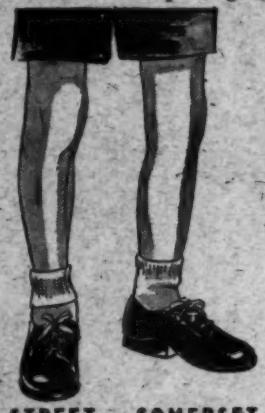

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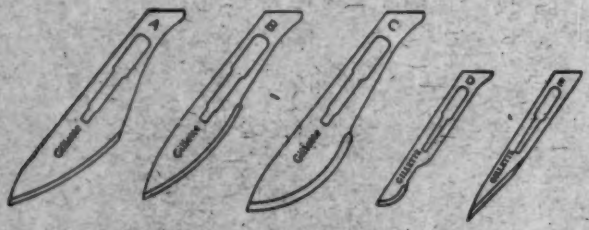

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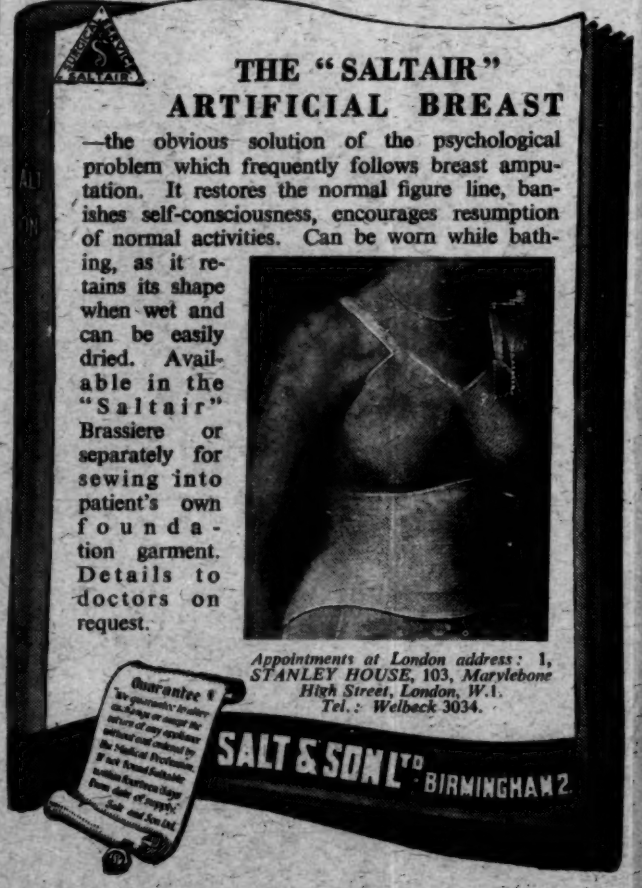

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY OCTOBER 28 1950

"VERITIES YET IN THEIR CHAOS"*

BY

CHARLES McNEIL, M.A., M.D., F.R.C.P., F.R.C.P.Ed.

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Thomas Hobbes, the philosopher, was a contemporary and familiar friend of William Harvey. Hobbes has described the life of man as "nasty, brutish, and short." He knew something both of life and of medicine. He had studied anatomy and read Vesalius in Paris; and he lived to the age of 90 by a health system of his own, and by keeping clear of doctors. A strong point in his system was exercise, and a favourite exercise was singing. This is described by Aubrey (*Lives of Eminent Men*): "At night when he was abed and the doors made fast, and was sure nobody heard him, he sang aloud (not that he had a good voice) but for his health's sake: he did believe it did his lungs good, and conduced much to prolong his life." Aubrey adds: "He seldom used any physique. He was wont to say that he had rather have the advice or take physique from an experienced old woman who had been at many sick people's bedsides, than from the most learned but unexperienced physician."

This story suggests the low state and repute of medical practice in 1602, when Harvey came back to London from Padua, like Portia, "a young and learned doctor." Yet he brought back with him from Padua the best medical science of that time. It was the system of Galen brought up to date: Galen's anatomy revised and added to by Vesalius and Fabricius; his physiology, hardly modified but brilliantly expounded by Fernel in his *Physiologia*. It was the physiology that specially interested the young Harvey, and that was to be his life-long study. There were the four elements and temperaments; the four humours; the three coctions; the three spirits derived from the three great organs—liver, heart, and brain. The blood, carrying nutriment to every part, flowed out and came back by the same vessels—veins and arteries: and the blood was also charged with innate heat. But almost nothing was known of the true function of the heart, lungs, brain and nerves, muscles, and digestion.

Although the human body with its great organs had been dissected for sixty years by the accurate standards of Vesalius, there was confusion and almost complete ignorance of how these organs worked. These humours and spirits and innate heat and the rest had truth in them; but they were dim shapes, "without form and void"; they were "medical verities yet in their chaos." And so pestilence raged, disease prevailed, and humanity suffered. Medicine was a learned science, but it was impotent in practice.

Harvey's Two Masterpieces

Harvey's life-work lay before him, a stretch of more than fifty years. His professional success as hospital physician, trusted official in his college, and physician to the Royal Court was rapid and distinguished. But what was extraordinary and immortal was his work as a thinker and discoverer; and the fruits of his genius were given to us in his two books, *De Motu Cordis et Sanguinis in Animalibus* (1628), and *De Generatione Animalium* (1651). the one appearing in the middle, the other towards the end, of his working life.

In both books the subject of study was physiology, the working of the human and animal body; and Harvey's general aim was a revision of the physiology of Galen. He wished, in fact, to bring out a new edition of this part of Galen's vast encyclopaedia of medicine, and for this immense task he chose his methods carefully. His first object was to bring data to "the cognizance of the senses": and he got these *sense*-data by anatomy—human anatomy, comparative anatomy in many kinds of animals, and experimental anatomy in living animals. Then, having got and verified his *sense*-data, he reasoned from them and tried to reach a physiological conclusion.

These famous Harveian methods seem to be paraphrased by Sir Thomas Browne, physician of Norwich and contemporary of Harvey, in a passage from his *Christian Morals*, the passage ending with the title of this address "Fly not only on the wings of Imagination: join Sense unto Reason, and Experiment unto Speculation, and so give life unto Embryon Truths and Verities yet in their Chaos." Reading Browne's lovely prose and admiring the beauty and antique charm of the words, one can miss the depth and truth of his thought. For this passage exactly describes the methods used by Harvey in his *De Motu*. There is the evidence of *sense* given by anatomy and experiment; the use of inductive reason and the element of speculation as to the missing link of the capillaries. These four mental instruments used together in *De Motu* drew out of chaos into clear form the verity of the circular motion of the blood.

De Motu is a masterpiece, announcing a great discovery, and showing a method applicable to every field of medicine

*Oration given at the 155th Festival, Harveian Society of Edinburgh, on June 2.

and science. His second book, *De Generatione*, takes a lower rank in physiology. Here Harvey was dealing with more complex problems where his instrument of anatomy was not fine enough to give him the necessary *sense*-data (he needed the microscope); he overloaded his argument with speculation, and, flying "only on the wings of Imagination," he often went astray. But it is a classic, and in some ways is a greater book; it deals with bigger problems, and shows Harvey in a wider range as biologist and metaphysician.

Harvey's Unwritten Books

In the closing chapters of *De Motu* Harvey shows that he had in mind other problems than the motion of the blood and heart; these other problems covered the whole range of Galen's physiology. Years before *De Motu* was written he was studying the function of the lungs and the whole problem of generation. He had now shown by carefully chosen methods that the motion of the blood was a circulation. This discovery opened a wide range of new problems which he could examine and might solve in the same way. Harvey, impatient and irritable in the ordinary intercourse of life, showed in the writing of *De Motu* a firm mind disciplined and calm. But in the second last chapter the thought of his discovery raises him to an unusual excitement: "Finally reflecting upon every part of medicine, physiology, pathology, semeiotics, and therapeutics, when I see how many questions can be answered, how many doubts resolved, and how much obscurity illustrated, by the truth we have declared, the light we have made to shine, I see a field of such vast extent in which I might proceed so far and expatiate so widely that this my tractate might swell out into a volume which was beyond my purpose, but my whole life would not suffice for its completion." This was only a dream, and the great enterprise does not seem to have been seriously taken up.

But in *De Motu*, in the Two Letters to Riolan, and in *De Generatione*, he gives a list and names the titles of seven treatises which he proposes to write and for which he has already made experiments and collected observations. The list is: (1) On the Causes, Uses and Organs of Respiration; (2) On the Formation of the Foetus; (3) The Organs of Motion (Heart and other Muscles); (4) Medical Observations and Pathology; (5) The Loves, Lusts, and Sexual Acts of Animals; (6) Physiology and Particular Treatise on the Blood; (7) On the Soul and its Affections. The only one of the list to be completed was "The Formation of the Foetus," published as *De Generatione*. The other six unwritten books of Harvey's may be called his hyperaemic (unprolific) eggs, conceived in his brain, undergoing some gestation there, but never brought to birth. The one most nearly completed was his "Medical Observations and Pathology," which, he says in his First Letter to Riolan (1649), "I intend putting to the press," and which in *De Generatione* (1651) he hopes to complete, "if God grants me longer life."

This grand review of medicine and physiology which Harvey planned in these unwritten books was beyond his powers, because the means of acquiring the new knowledge were not available in his time. This rewriting of Galen's system of medicine and surgery was to be done not by one but by many men, written slowly page by page not in a single generation but over three hundred years; and the great volume is not finished yet. But about Christmas, 1650, Harvey handed over, rather reluctantly, to his friend, Dr. George Ent, the manuscript of *De Generatione*, and this great and strange book was published in 1651.

Harvey's Doctrine of the Soul

De Generatione contains seventy-two exercises on conception and development; and added essays on parturition, the uterine membranes and fluids, and his final theory of conception. But, mingled throughout, there is also much general biology, and, what is strange and disappointing to modern biologists, much metaphysical argument dealing with the soul. The book contains many references to his planned but unwritten treatises, and many passages showing his fine sense of poetry. It is an extraordinary book, interesting to read but not easy to understand, and it shows the range and depth of Harvey's mind. Even its mistakes, the mistakes of a great mind, are worth consideration. It made no substantial contribution to the physiology of development. But it firmly stated the doctrine of epigenesis as opposed to metamorphosis—a doctrine which was amply confirmed much later by Wolff and von Baer; and its influence upon the improvement of midwifery practice has been made clear by Professor R. W. Johnstone in his Oration to our Society two years ago. It again shows Harvey, as in *De Motu*, a great and accurate anatomist and a tireless and ingenious experimenter.

In it he reaches his full stature as a general biologist, dealing with all living creatures, man and animals, birds, fishes, insects, and plants—as Newton said of himself, "gazing at the ocean of being that lay before him." And for Harvey, in his study of being, there was something beyond biology, although joined with it. With this mysterious *beyond* Harvey's mind wrestled, and so in *De Generatione* Harvey passes from biology into metaphysics, and states his doctrine of the soul and the blood, of the soul in man and animals, and of the Soul of the Universe.

Harvey's mind and outlook were formed at Padua. Here he was trained in anatomy by Fabricius; he may well have heard the new teaching in physics by Galileo; and he came into deep contact with the towering mind of Aristotle ("master of them that know"), and read the Aristotelian treatises on biology, generation, and metaphysics. According to Aristotle and most of the great thinkers up to Harvey, there was in the living body something more than physical structure and physical process; and so alongside physics as a subject of study there lay metaphysics. Harvey had no shadow of doubt about this; and so he shows himself in *De Generatione* both as biologist and as metaphysician, and discourses again and again of the soul, how it is joined to the body, and how together they make up the lives of man and animals.

The Soul and the Blood

Harvey's final position was that the immediate link between soul and body was the blood. Throughout his life his mind was fascinated by the blood. In *De Motu* he had taken up and solved the path of the blood and the action of the heart in maintaining its circular course: and, following Aristotle, he at first gave primacy in the whole body to the heart, saying: "It is the heart by whose virtue and pulse the blood is moved, perfected, made apt to nourish, and preserved from coagulation and corruption . . . [it] is indeed the foundation of life, the source of all action." But in *De Generatione* he has changed the emphasis from the heart to the blood, and he now puts the blood in the first place. He did this because, in his study of the early development of the hen's egg, he was satisfied that the blood appeared before the heart and every other organ and part. This appearance was the famous punctum saliens of Aristotle. This first sign of animal life

in the 4-day-old chick as a red "leaping point" had been seen nearly two thousand years before by Aristotle, who named it punctum saliens and proclaimed it to be the heart of the embryo chick.

Harvey confirmed the observation of Aristotle, but with a significant difference. This is Harvey's vivid description, given in the first English translation of *De Generatione* (1653). "If therefore you observe on the fourth day, you will meet a great metamorphosis and wonderful alteration, which are more evident almost every hour that day long: about which time the Egg beginneth to step from the life of a Plant to the life of an Animal. For now the Limbus or hemme of the colliquamentum beginneth to blush and purple, being encompassed by a slender bloody line: and in the centre almost of it, there leapeth a capering bloody point [Aristotle's punctum saliens] which is yet so exceeding small that in its diastole or dilatation it flasheth only like the most obscure and undiscernable spark of fire, and presently upon its systole or contraction it is too subtile for the eye and quite disappeareth." After careful and repeated observation Harvey was convinced that the red line (the embryonic blood) appeared *before* the red leaping point, and he therefore now transferred to the blood the primacy in the life of the body. He puts his new view plainly: "The blood is the prime part engendered, and the heart the mere organ destined for its circulation."

Continuing his study of the blood, he next takes up the old doctrines of Galen of humours and many kinds of spirits working in the blood, and of the innate heat; and dismisses them all with scorn: "Nothing is more uncertain and questionable than the doctrine of the spirits . . we have found none of all these spirits by dissection. . . There is in fact no occasion for searching after spirits foreign to or distinct from the blood, to evoke heat from another source, to bring gods upon the scene, and to encumber philosophy with fanciful conceits; what we are wont to derive from the stars is in fact engendered at home; the blood is the only innate heat." With the ground cleared, he goes on to describe the powers and properties of the blood in relation to the soul and the processes of animal life. "It [the blood] is the common bond between soul and body: it is the immediate instrument and principal seat of the soul . . . it is the instrument of the Great Workman . . . it is to be regarded as the substance whose act is the soul or the life . . . it therefore comes to the same thing whether we say the soul and the blood, or the soul with the blood, or the blood with the soul, performs all the acts in the animal organism."

This is Harvey's doctrine of the soul and the blood. It replaces the many spirits and innate heat of Galen with one spirit, the soul, which performs through the blood all the acts of life. It does not tell how the acts of life are performed; elsewhere he says that these operations "are carried out with such foresight and divine intelligence which indeed surpasses our understanding, and are in no way to be penetrated by the dull edge of our apprehension." With him physiology has now ended and metaphysics has begun; unable to search out physiological *process* any further, he goes on to speak of *cause* in man and in the universe. The soul of man, interfused through his blood and body, is linked with and dependent on "the first cause of all things, by whatever name this has been designated—the Divine Mind of Aristotle, the Soul of the Universe by Plato, the Natura Naturans by others." In the same argument he turns to and quotes his beloved Virgil—"in the same way as in the greater world we are told, 'All things are full of Jove—Omnia plena Jovis,' so in the slender body of the pullet, and in every one of its actions, the finger of God or Nature obviously appears."

This last sentence and many like it have the feeling if not the form of poetry, and show Harvey as poet as well as metaphysician. He did not express his thought in verse, but when he rises to the height of his argument he shows the true sense and quality of poetry. He combined anatomy and poetry—a strange combination. Anatomy divides, dissects, and looks at parts. Poetry looks at things undivided and whole, and, however small the thing is, in its widest relations. And poetry is also and essentially metaphysical. Its language is not that of metaphysics, for it uses words that are understood by all men, even the unlettered. In poetry deep is speaking unto deep; and this deep is the soul in man. The universal range and poetical quality of Harvey's thought are shown in this passage where he is speaking of the nesting of birds: "And it is indeed a thing most worthy of admiration to see these creatures selecting and preparing their nests with so much foresight fashioning and furnishing, and concealing them with such inimitable art and ingenuity, so that it seems imperative on us to admit in them a certain spark of the divine flame (as the poet says of bees)."

Fulfilment in Physiology and the Liquidation of the Soul

Three hundred years have gone since *De Generatione* was published. Harvey brought no more unfinished books to press, and died in 1657. In this long march of time, the medical *comoedia* has moved upwards, slowly but very far, from the inferno of unknown and uncontrolled disease in which it lay in Harvey's day; and this progress has been mainly due to the building up of physiology. The effort and achievement of one man are of little account compared with this gigantic task and the many who have helped to complete it. But Harvey was a Titan among men, both in his power of mind and in what he set himself to do. He gave the new physiology a splendid start in his discovery of the circulation, but beyond that he added little. Looking back, we can see the reason for his failure. He had to hand the two instruments of anatomy and the experimental method; and his anatomy, consisting of dissection, his trained eyes, and the occasional use of the magnifying glass, was not fine enough. But the range and penetrating power of anatomy were to be prodigiously increased by the gradual perfection of physics and chemistry. Optical physics soon produced the microscope, and much later the *x* ray; electrical physics; and the fine filter: all these inventions gave really a finer and deeper anatomy, put at the disposal of physiology. So also the perfection of chemistry, essentially a sublime anatomy, revealed the intimate and ultimate structure of cells and fluids and their components.

In the closing years of Harvey's life anatomy was becoming microscopical, and three years after his death Malpighi with his microscope saw blood flowing in the capillaries, and supplied the missing link in the circular chain of the blood. A few years later the microscope showed red corpuscles in the blood and spermatozoa in the seminal fluid. These were only the first fruits of a rich harvest to be reaped by the microscope: but these three discoveries all touched on, adding to or correcting, Harvey's work on the blood and generation.

About the same time, and in London, the new physics attacked the baffling problem of respiration. Boyle, Hooke, Lower, and Mayow demonstrated a new kind of "spirit" in the blood derived from the in-breathed air. This was called "igneo-aerial spirit," and after two hundred years

of further search it was isolated and named oxygen by Lavoisier. Innate heat and igneo-aerial spirit are akin in name and in nature: the one is the "embryon truth" of Galen; the other its further development, coming to maturity in the modern doctrine of oxidation and combustion. As for Galen's humours and spirits, the new chemistry has found the blood and body fluids to be teeming with humours, ferments, hormones, and spirits in greater numbers and complexity than Galen and Fernel imagined.

Harvey, you will remember, dismissed the doctrines of the spirits and innate heat, saying that *his* "dissection could show nothing of the sort." He emptied the old chaos of shadowy spirits, and into the void that was left he introduced the metaphysics of the soul, carrying out, through the blood, all the processes of life. The more perfect *dissection* of the microscope and of physics and chemistry has shown Harvey to have been wrong, and that Hippocrates and Galen have been justified by their modern children in physiology. The old Greeks were men of genius, and their guesses, vague and without form, were a dim foreshadowing of truth. Their doctrines, rejected by Harvey, were "verities yet in their chaos"; they have now come out of their chaos and stand in clear and delicate outline as chemical and physical processes. It is not beyond the mark to say that modern physiology is a new edition of the old Galen, revised, rewritten, and greatly enlarged.

Biology and Metaphysics

And how has it fared with Harvey's doctrine of the soul and the blood, and of the soul generally? We can see what happened to Harvey in his study of the blood. He was a profound student both of biology and of metaphysics. His instruments for the study of the blood and of biology in general were anatomy and experiment. But his instrument of anatomy was not fine enough; and, having got from it all that it could do, he took up metaphysics. This combination of biologist and metaphysician was now becoming dangerous.

Descartes, philosopher, brilliant amateur of physiology, and contemporary of Harvey, gave in his writings a firm warning that, in the study of man, the soul and the body, metaphysics and biology, should be kept apart. Since this warning was given most biologists have taken the lesson to heart and have fought shy of metaphysics. In their study of living bodies they have done what Descartes advised, and have used only physical methods, and have stated their results in strictly physical terms. In this concentration on physics and exclusion of metaphysics they have in three hundred years filled the void of Galen's physiology with a labyrinth of living processes, working under physical and chemical laws, and in so doing they have made the practice of medicine powerful and beneficent.

Indeed, biologists have gone beyond the lesson of the master. Finding the most intimate processes of life to be explained by chemistry and physics, and finding nothing else in life but chemical operations, they see no place in the living body for metaphysical spirit. They might well use Harvey's own words: "There is no occasion for searching after spirits . . . to bring gods upon the scene . . . to derive from the stars what is in truth engendered at home." Life, we are told, is a form of matter; and living matter is chemistry in action. The biologists have gained the whole world in physiology, and have lost the soul. Sir Charles Sherrington, in his deep, scholarly, and humane study, *The Endeavour of Jean Fernel* (1946), has concluded a fine commentary on the old physiology thus: "To-day physiology *is* chemistry and physics," and he calls for "the liquidation" of the life-soul and the other forms of spirit on Fernel's list.

It seems a hard and severe sentence; but the biologists have an old-standing grievance against the metaphysicians, and are not prepared to show mercy on their doctrines. They say that the metaphysicians, meddling with biology, have retarded its progress. Harvey's activities as a metaphysician they pass over in silence, or with an expression of mild regret, because in his case there are extenuating circumstances in his great physiological discovery of the circulation. And it must be granted that Harvey in his studies of the blood and male seminal fluid was in serious error, and allowed his doctrine of the soul to usurp the place of physiology. But he made fundamental statements about the rational soul in man and the Soul of the Universe—statements which in this general form have been held by the great majority of mankind in all recorded time and which have been the mainstay of their thought and action. Is this great doctrine of soul or spirit now to go into liquidation?

This great question cannot be dealt with now; but, with Harvey's affirmations about the soul in our mind, it can be looked at in its broad significance and implications. It is more than a question of doctrine for debate between biologists and metaphysicians; it is of deep concern for all men in their daily lives.

Life Without Soul

This new, or rather old-new, theory of life without soul promises great benefits, but it seems to carry practical losses and risks. The biologist tells the ordinary plain simple man to forget the old fairy-tales about spirit and to accept the new and true chemical story about life, and the dialogue goes on:

Biologist: "The world, yourself, even your thoughts, all are a marvellous chemistry which has been operating the whole universe of things alive and dead, and for thousands of years past until now."

The Plain Man interrupts with a question: "Must there not be a great Chemist, who has made all this chemical stuff, and who directs this tremendous chemical operation?"

The Biologist: "That question raises the old hare of the First Cause, and I am not going to chase it. Such a question is beyond chemistry. In any case, you don't *need* a First Cause; and I can give you all you do need. As yet I can't make the stuff; but my power of destroying it gets greater and greater. I have come to know most of the secrets of the chemistry. So far as you are concerned, I am the manager; and if you do what I tell you I shall give you in abundance everything necessary for your life—every chemical need. But all this nonsense about spirit, you must cut it out of your life—to use a good chemical term, you must liquidate it."

The Plain Man: "About music; must I give up the spirit in my music?"

The Biologist: "There is a good story about an old man. Thomas Hobbes, who sang himself to sleep every night, singing out of tune and without spirit. His music was mainly chemical—noise and exercise, and for a chemical end—the promotion of his health, and yet his music without spirit helped him to live till the age of 90. Isn't that good enough?"

The Plain Man: "The loss of soul in music would be a heavy one for me. Another question: What about poetry, which means a great deal to me?"

The Biologist: "Poetry is full of soul-stuff too: its essence is spirit. Poetry would keep alive the false doctrine of spirit, and would have to be repressed or severely controlled."

The Plain Man: "This would be a dreadful loss. One more question: What about religion in the new chemical world?"

The Biologist: "Religion is a fairy tale which must be told no more, not even to your children. You are a grown man

now; and you can and must do without it. Religion must go: it has done you grievous harm."

At this the plain man drops his head and is silent.

The Biologist (continuing): "Only look at what I have to offer you in exchange for your soul. In the language of an old book which you seldom read and which is now obsolete, I will pull down your old barns and build you bigger and better ones; and I will fill them to the roof with 'goods' that our newest chemistry will provide—food, clothing, health, long life, ease, and pleasure. The loss of your soul is nothing to what you will gain."

The Plain Man: "What you offer tempts me. Many of us plain folk need these chemical goods badly. But the idea of life without soul frightens me; it would be so flat and cold and dreary, and it might be dangerous. We have always been told that our souls are the best part of us. And yet your best chemists have searched every corner of us, and have found no chemical trace of soul. Could it not be that soul is of different and non-chemical stuff, that if you used other long-tried non-chemical methods of search, at once and everywhere, within our bodies and without, you would find soul?"

Conclusion

To sum up: Harvey's discovery of the circulation of the blood was the beginning of a new chapter in physiology. It may be compared to the appearance of the punctum saliens in the 4-day-old chick; "like a spark darting from a cloud" (his own words), it was the first sign of new life in European physiology, and was followed in a kind of epigenesis by a succession of other discoveries. Much of what he wished to do he left undone; but his unfinished work has been brought to fulfilment by others, and the verities of physiology are now no more in their chaos.

As to his teaching on the soul, both his particular doctrine of the soul and the blood, and his general statement of the soul in man and in animals, and the Soul of the Universe—all this has been rejected by modern biology. But biology has not said its last word, and is struggling even now to find its own metaphysic on the question of cause. Meantime Harvey's general statement on the soul is worth setting alongside those of other great minds in ancient times. *The Book of Wisdom*: "The Spirit of the Lord hath filled the whole earth." Aristotle: "All things are full of Soul." Virgil: "All things are full of Jove." Last, Harvey, speaking as a biologist: "For, as the same intelligence or spirit which incessantly actuates the mighty mass of the Universe . . . so also is there a *vis enthea*, a divine principle, inherent in our common poultry."

At the third annual general meeting of the British Rheumatic Association held on September 28 it was reported that the association is now established as a national organization and a registered charity. It maintains helpful connexions with the Ministry of Health and regional hospital boards. As the result of these, spa treatment can now be authorized under the National Health Service by a consultant in rheumatism, and those who can find their own accommodation can be treated as out-patients in any hospital rheumatic unit, subject to the recommendation of their own doctor and a recognized consultant. To meet the difficulties of rheumatics in finding accommodation close to centres where they can get urgently needed treatment, the association has promoted the formation of a housing society with charitable status under the title of B.R.A. Homes Limited to provide accommodation on a voluntary basis. Another of its activities is to provide flatlets for the old and disabled rheumatics within a certain income group. This will make it possible to combine geriatric with rheumatic treatment, which recent experience shows can relieve pressure on hospital beds.

ANTICOAGULANTS IN TREATMENT OF CORONARY THROMBOSIS

BY

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Adequate care for the patient suffering from acute coronary occlusion is one of the most urgent problems in present-day therapeutics. A disease which statistics prove to be on the increase, which is afflicting younger lives (Ryle and Russell, 1949), and which after 25 years' study can still be shown to have a mortality rate of 40% among hospital patients within the first six weeks, is a challenge that for too long has been neglected.

Myocardial infarction, the result of coronary artery occlusion, now constitutes a large part of cardiological practice. The exact incidence of the condition throughout the general population is difficult to assess. All grades of severity are encountered, from the most severe cases dying immediately or within a few minutes or hours from the onset, to the very mild which experience little upset and have no ensuing disability. It is therefore the moderately severe or the complicated cases which provide the greater part of hospital experience. Statistics gathered from the hospitals cannot be applied to the population as a whole, but in this disease they certainly indicate the course followed by the moderately severe case treated, as we believe, under the best available conditions.

A study of the literature indicates that the immediate mortality following myocardial infarction varies widely in different centres and perhaps in different hospitals in the same city. In Table I the mortality rate ranges from the

TABLE I.—*Showing how the Mortality Rate Varies in Different Series of Patients in the First Few Weeks After the Acute Occlusion*

Author	No. of Cases	Mortality %	Remarks
Levine and Brown (1928) ..	145	53	
Conner and Holt (1930) ..	284	16	First attacks only
Harrington and Wright (1933) ..	148	54	
Master *et al.* (1936)	267	17	
" " (1937)	140	21	
Bland and White (1941) ..	200	19	4-weeks period
Levine and Rosenbaum (1941) ..	208	33	
Woods and Barnes (1941) ..	128	47	
Newman (1946)	50	78	Young adults
Katz and Mintz (1947) ..	572	22	
Yater *et al.* (1948)	866	52	Young adults; 4-weeks period
Wright *et al.* (1948)	368	24	

78% of Newman (1946) to the 16% of Conner and Holt (1930). Our current Edinburgh experience has been assessed from two series of hospital patients, the first being composed of 100 consecutive cases of coronary thrombosis observed during the period 1939–46, before the introduction of anticoagulants; their mortality rate was 43%. A second series of 84 consecutive patients, forming the present control group and observed concurrently with a similar number receiving anticoagulants, had a mortality rate of 41%. Through the courtesy of physicians elsewhere in

*Work done during the tenure of a Grocers' Company Research Scholarship, 1947–9.

this country—Dr. Boyd Campbell, Dr. J. H. Wright, and Professor Crighton Bramwell in personal communications—we are able to report hitherto unpublished mortality rates for hospital-treated cases of coronary thrombosis in Belfast, Glasgow, and Manchester. The findings, presented in Table II, indicate that, in the absence of any specific therapeutic measures, coronary thrombosis has a mortality rate in the neighbourhood of 33% among hospital patients in this country.

TABLE II.—*Presenting Recent Experience of Mortality Rates After Coronary Thrombosis at Four Centres in this Country. Anticoagulants were Not Employed in the Treatment of These Patients. The Figures Indicate that Among Hospital-treated Patients 33% is an Average Mortality Rate During the First Six Weeks*

Locality	No. of Patients	No. of Deaths	Mortality %
Belfast (Boyd Campbell)	169	50	30
Glasgow (Wright, J. H.)	100	25	25
Manchester (Bramwell, C.)	50	13	26
Edinburgh: This series (*a*)	100	43	43
„ „ (*b*)	84	34	41
Total	503	165	33

Embolic and thrombotic episodes, which may handicap a convalescent patient or prove immediately fatal, are common after myocardial infarction. Such episodes comprise: (1) the sudden occlusion of a systemic artery; (2) the development of a fresh myocardial infarct or the spread of the occlusive process to adjoining branches of the affected artery, and hence an extension of the original damage; (3) peripheral phlebothrombosis, notably in the calf veins; and (4) pulmonary infarction. In recent years a much higher clinical incidence for thrombo-embolic phenomena after coronary occlusion has been recorded, suggesting that in earlier reports minor episodes had been overlooked. This is demonstrated in Table III. Mural thrombus formation on the endocardial surface of the infarcted area of the ventricle is present in 44% of necropsy cases, but all peripheral arterial occlusions are not necessarily embolic in origin (Hellerstein and Martin, 1947). It is during the first three weeks after the acute occlusion that thrombo-embolic incidents are most apt to occur (Nay and Barnes, 1945), and it is during this same period that an upset in the control of intravascular blood-clotting has been demonstrated (Ogura *et al.*, 1946). Using the Waugh-Ruddick (1944) heparin-retarded clotting test, Ogura and his colleagues observed the development of an enhanced clotting tendency in 75% of cases of recent myocardial infarction. An increased coagulability of the blood appeared during the first week, reached a maximum towards the end of the second week, and disappeared during the third week. Our own experience has been that there is considerable individual variation in the time of onset, duration, and degree of this change.

TABLE III.—*Showing that the Frequency with Which Thrombo-embolic Incidents after Coronary Thrombosis are Recognized has Apparently Increased in Recent Years*

	Authors	No. of Cases	No. with Thrombo-embolic Episodes
A. Early series	Gordinier (1924)	13	3
	Anderson (1928)	9	1
	Parkinson and Bedford (1928) ..	100	8
	Levine and Brown (1928) ..	145	17
	Conner and Holt (1930)	287	42
	Hyman and Parsonnet (1931) ..	51	17
	Howard (1934)	165	17
	Blumer (1937)	175	27
	Master *et al.* (1939)	500	29
		1,445	161 = 11·1%
B. Recent series	Nay and Barnes (1945)	100	37
	Peters *et al.* (1946)	60	10
	Glueck *et al.* (1948)	44	27
	Greisman and Marcus (1948) ..	100	21
	Wright *et al.* (1948)	368	92
		672	187 = 27·8%

In the treatment of myocardial infarction the possibility of controlling this enhanced clotting tendency and preventing thrombo-embolic complications appeared attractive. The introduction of the anticoagulant dicoumarol made this supposition a practical measure. The earliest reports on anticoagulant therapy by Wright (1946) and Peters *et al* (1946) indicated that not only was the incidence of thrombo-embolic complications greatly lessened, but the immediate mortality rate was strikingly reduced. With the accumulation of further reports in the American literature, supplemented by the large-scale investigation at 16 leading hospital centres sponsored by the American Heart Association, the evidence is overwhelmingly in favour of this method of treatment. Table IV, constructed from American statistics, suggests that anticoagulants are capable of reducing the mortality rate by one-half.

TABLE IV.—*Constructed from Reports in Recent American Literature. Contrasts Mortality Rates in Cases Treated With and Without Anticoagulants. The Mortality Rate is Apparently Halved by the Use of these Drugs*

Author	Anticoagulant Cases		Control Cases	
	Total	Deaths	Total	Deaths
Wright (1946)	76	15	—	—
*Peters *et al.* (1946)	50	2	60	13
Nichol (1947)	68	11	—	—
Parker and Barker (1947) ..	50	5	—	—
*Greisman and Marcus (1948)	75	7	100	35
Glueck *et al.* (1948)	44	9	44	20
Reich and Eisenmenger (1948) ..	30	4	—	—
*McCall (1948)	71	9	—	—
Wright *et al.*.. (1948)	432	65	368	88
Hilton *et al.* (1949)	38	5	76	18
Loewe and Eiber (1949) ..	20	1	—	—
	954	133	648	174
Mortality rate ..	13·8%		26·8%	

* Cases dying within 48 hours of admission are not included.

Whether all cases derive equal benefit has not been adequately investigated. Wright *et al.* (1948) indicated that males aged 60 years and over showed greatest improvement, and Greisman and Marcus (1948) in a small series reported a greater improvement among males than among females. The present investigation, now to be reported, was begun in 1947 with the object of assessing the value of anticoagulant therapy in myocardial infarction and of determining, if possible, the type of case most likely to benefit from this form of treatment.

Material

During the past three years 154 cases of myocardial infarction have been observed and treated. These comprise two series of cases: one series, consisting of 84 cases, was treated by conventional conservative measures and constitutes the "control" series; the second series, consisting of 70 cases, received anticoagulant therapy during the first three weeks after admission in addition to the standard forms of treatment, and constitutes the "treated" series. All cases were unselected, their inclusion in one or other series being determined by the day of their admission to hospital. All cases admitted to one medical block were treated conservatively, whereas all cases admitted to a second block received anticoagulants—unless some contraindication to their use existed. Both series comprise, therefore, the

everyday emergency admissions to a medical ward. No case was admitted specifically for anticoagulant therapy. All cases admitted and dying within six hours of admission have been excluded from both series, as insufficient time had elapsed for any benefit to result from the treatment given.

Diagnosis was based on the history and the usual signs, supported by positive electrocardiograms in 134 of 136 patients thus examined, and by the course of the illness. Cases in which a doubt existed regarding the presence of a recent myocardial infarct have been rigorously excluded from the series under review.

Treatment

The routine treatment adopted for all cases consisted in rest in bed for five to six weeks, morphine for relief of pain, sedation with phenobarbitone, low calorie intake, graduated exercises from the fourth week, and treatment of complications as and when they arose. The "treated" series received in addition heparin and dicoumarol (64 cases) or dicoumarol alone (6 cases). Heparin was given by the interrupted intravenous injection method, the interval between injections being 8 hours in 62 cases and 6 hours in two cases, the latter two cases having both experienced thrombo-embolic complications before their admission to the ward. Except in the first few cases, each injection consisted of 10,000 units of heparin. Adequacy of dosage was assessed by estimation of the clotting time one hour after the injection, using the Lee–White (1913) method. A time of 20 minutes, three or four times the normal value, was regarded as satisfactory. The injections of heparin were stopped as soon as a therapeutic reduction in prothrombin content had been achieved with dicoumarol. The object in using the latter drug was to obtain a prothrombin content less than 30% of normal (Allen, 1947). This level was seldom attained before the fourth or fifth day of treatment. Dicoumarol was therefore started on the day of admission, the dose being 300 mg. on the first day, 200 mg. on the second day, and 100–200 mg. on the third day. All subsequent doses of dicoumarol were determined in relation to the daily estimation of the prothrombin time. The Fullerton (1940) modification of the Quick method, using venom as the source of thrombokinase, was the technique employed. It was appreciated that at low concentrations of prothrombin this method is less sensitive than the original Quick method in detecting minor variations in prothrombin content, but the same technique was used throughout this series.

The daily dose of dicoumarol was regulated approximately by the following guide: using a control prothrombin time of 19 seconds, 100–200 mg. of dicoumarol was given if the patient's prothrombin time was under 28 seconds, but if the prothrombin time was over 28 seconds a dose of 0–100 mg. was given. In regulating the dicoumarol dosage, Wright (1950) commends the Sterling Nichol formula whereby the ideal prothrombin therapeutic level is maintained between two and two-and-a-half times the control prothrombin-time for that day in the laboratory (Nichol and Borg, 1950). It is important to note that, unfortunately, there is no clinical guide to the regulation of dosage with this drug. Individuals vary greatly in their susceptibility to it, and the appropriate dose on any one day can be ordered only when the laboratory has reported on the prothrombin-time existing on that date. Patients given dicoumarol without laboratory control may bleed heavily. Even 150 mg. daily may lead to serious haemorrhage in a short period of time.

A minimum period of three weeks of dicoumarol therapy was decided upon for three reasons: (1) the great majority of thrombo-embolic phenomena occur during that period; (2) the clotting tendency previously mentioned tends to disappear towards the end of the third week; and (3) the effect of dicoumarol persists for several days after administration of the drug has ceased.

In this series the total dicoumarol dosage in the three weeks of treatment ranged from 1,100 mg. to 4,200 mg., the majority of cases receiving 2,000 to 3,000 mg. Haemorrhagic complications were treated by stopping the drug, and, if severe, by administration of vitamin K, 50 mg. intravenously as a single dose, with 100 to 150 mg. daily by mouth.

Comparison of Two Groups

Before drawing any conclusions regarding the efficacy of anticoagulant therapy it is necessary to compare the two series of cases in respect of similarity in important details. The immediate prognosis in myocardial infarction depends on a number of factors, which should be equally distributed between the two groups. Both series have therefore been analysed in respect of (1) age, (2) sex, (3) pre-existing hypertension, (4) pre-existing angina pectoris, (5) number of previous myocardial infarcts, (6) obesity, (7) myocardial state prior to the infarct, (8) duration from onset of symptoms to admission to hospital, (9) degree of shock at the onset, (10) incidence of heart failure, thrombo-embolic phenomena, and arrhythmias after the infarct, and (11) mortality rate within the first six weeks after the infarct.

Details of the age and sex incidence are given in Table V.

TABLE V.—*Presenting Details of the Age and Sex Incidence of the 154 Cases of Coronary Thrombosis Comprising the Present Series. The "Control" Series Consisted of 84 Patients and the "Treated" of 70 Patients Receiving Anticoagulants*

Age	Male				Female			
	Total		Died in Ward		Total		Died in Ward	
	Control	Treated	Control	Treated	Control	Treated	Control	Treated
35– ..	1	1	1	—	—	—	—	—
40– ..	—	2	—	—	—	—	—	—
45– ..	9	4	1	—	1	—	—	—
50– ..	5	11	1	1	1	2	—	2
55– ..	8	8	2	1	6	1	4	—
60– ..	15	13	4	3	8	10	5	2
65– ..	9	3	3	1	7	9	4	5
70– ..	6	4	5	1	4	2	1	—
75+ ..	1	—	1	—	3	—	2	—
Total	54	46	18	7	30	24	16	9

In the control series the males averaged 60 and the females 64 years of age, while in the treated series the males averaged 57 and the females 64 years. So far as sex and age distributions are concerned, it appears that the two samples —control and treated—are sufficiently homogeneous to warrant comparison. As shown in Table VI, the incidence of hypertension and previous angina pectoris did not differ widely in the two groups, though the incidence of obesity

TABLE VI.—*Showing that the Incidence of Hypertension and Previous Angina Pectoris did Not Differ Widely Between the Two Groups, Though the Incidence of Obesity was Almost Twice as Great in the "Treated" Series*

	Male		Female	
	Control	Treated	Control	Treated
Previous hypertension	33 (61%)	24 (52%)	16 (53%)	19 (79%)
Previous angina	16 (30%)	20 (43%)	14 (47%)	15 (62%)
Obesity	12 (22%)	19 (41%)	12 (40%)	18 (75%)

Table VII.—*Showing that Multiple Attacks of Coronary Thrombosis had been More Commonly Experienced in Those Receiving Anticoagulants*

	Male				Female			
	Total		Died in Ward		Total		Died in Ward	
	Control	Treated	Control	Treated	Control	Treated	Control	Treated
First ..	48	32	16	3	27	16	14	7
Second	6	10	2	3	2	3	1	1
Third	—	3	—	—	1	3	1	1
Fourth	—	1	—	1	—	1	—	—
Fifth ..	—	—	—	—	—	1	—	—

was almost twice as common in the treated series. Table VII demonstrates that multiple attacks of coronary thrombosis had been more commonly experienced in the treated series. One remarkable woman among those receiving anticoagulants had survived five myocardial infarcts.

In all cases in which a satisfactory history was obtained an attempt was made to gauge the state of the myocardium before the onset of the acute coronary occlusion. In some patients the attack was preceded for months or years by definite angina of effort; others had had no exertional pain but were restricted by dyspnoea; others again admitted to no cardiac symptoms previous to the occlusion. By applying the standards of functional capacity adopted by the New York Heart Association (1939) we placed our patients in the following broad categories:

Grade I patients are symptom-free, ordinary physical activity causing no discomfort.

Grade II A patients experience a slight-to-moderate limitation of physical activity. Walking on the flat out of doors at an average pace constantly reproduces ischaemic pain or dyspnoea after a few hundred yards.

Grade II B patients have a moderate-to-great limitation of activity. Less than ordinary activity causes discomfort. In this group we include those people who experience angina on light household activity or walking 20 to 50 yards out of doors, and those who have recurrent spontaneous attacks at rest, perhaps awakening them from sleep.

Grade III patients are those unable to carry on any physical activity without discomfort. As a rule they are confined to bed, congestive failure in some form being already present.

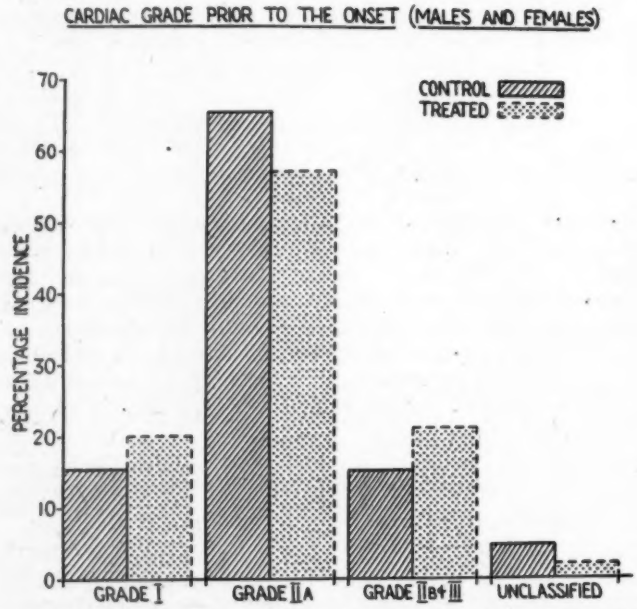

Fig. 1.—Incidence of various grades of functional capacity of the heart existing in the two series of cases of coronary thrombosis, previous to the onset of the acute occlusion. There is little difference between the "control" and the "treated" cases.

In applying this rough-and-ready measure of cardiac efficiency, we regarded symptoms developing comparatively suddenly during the two weeks immediately preceding the infarction as premonitory in nature and have not taken them into account in assessing the cardiac grade. The incidence of the various grades, which are evenly distributed between the two series, is shown in Fig. 1. Only in the treated series were there patients actually in congestive heart failure prior to the infarct.

For statistical purposes it is difficult to grade cases of myocardial infarction according to their severity. Clinically, the actual size of the infarct cannot be determined with much precision, nor does its extent determine the degree of shock. In an admittedly arbitrary fashion, the grade of shock, expressed according to clinical experience as severe, moderate, and mild or absent, may be taken as a measure of the severity of the illness. In a number of patients admitted some days after the onset the degree of shock could not be estimated, but Fig. 2 shows that the

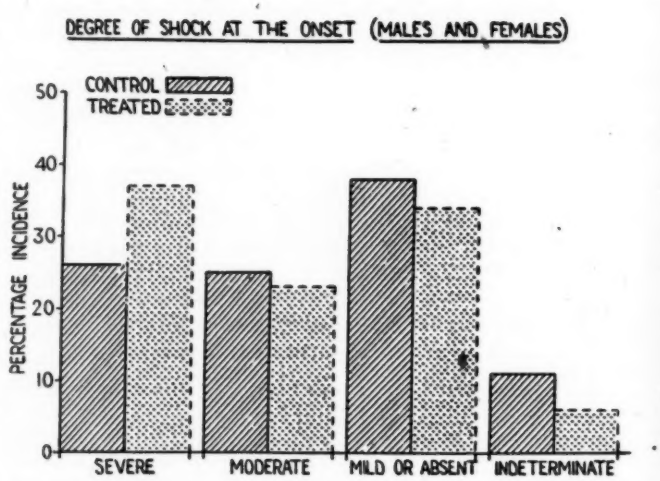

Fig. 2.—When the degree of shock is taken as a rough-and-ready measure of the severity of the attack of coronary thrombosis, the three grades—severe, moderate, and mild—were fairly evenly distributed between the two groups of patients.

three grades were fairly evenly distributed between the two series, with a preponderance of more severe cases in the treated group.

Finally, in the estimation of comparative mortality rates a further and commonly neglected factor has to be taken into consideration. A moment's reflection indicates that the mortality rate in a hospital series of cases of coronary thrombosis will be all the less the greater the delay in securing admission. It is known that the mortality rate in coronary thrombosis is highest in the first few days, and therefore the longer patients are excluded from the hospital the lower will be the death rate for the series, the more severe cases dying before admission. When the duration of illness before admission to hospital is compared, the two series—control and treated—are strikingly similar. 32% of the former and 34% of the latter arriving in hospital within 24 hours of the onset of the coronary occlusion (Fig. 3). Our two groups bear a close resemblance in this respect.

We may therefore conclude that the two samples—control and treated—in respect of sex and age distribution, pre-existing state of the heart muscle, severity of the acute attack, and duration of the illness before hospital treatment, are sufficiently homogeneous to warrant comparison.

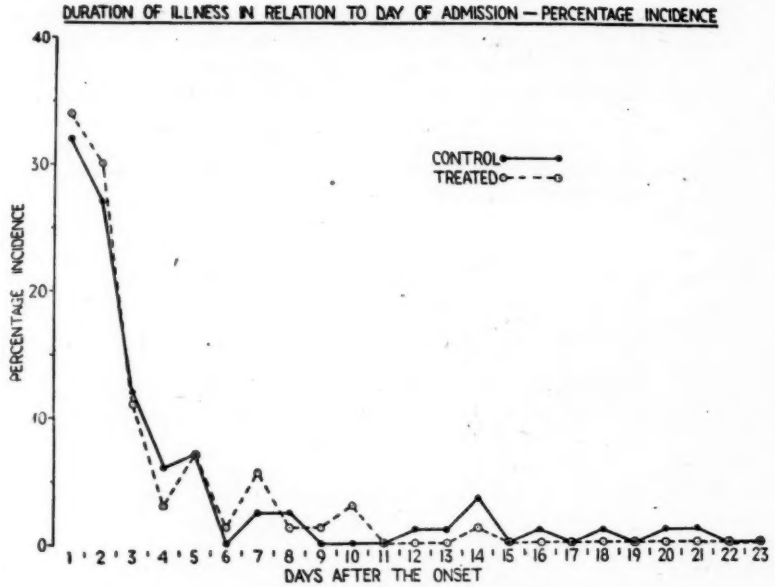
DURATION OF ILLNESS IN RELATION TO DAY OF ADMISSION — PERCENTAGE INCIDENCE
PERCENTAGE INCIDENCE
CONTROL
TREATED
DAYS AFTER THE ONSET

FIG. 3.—The duration of the illness as measured from the time of onset until admission to the ward is strikingly similar in the two groups, 32% of the "controls" and 34% of the "treated" arriving in hospital within the first 24 hours.

Results of Anticoagulant Therapy

In as severe an illness as coronary thrombosis it is natural to assess the results of treatment on the basis of (1) mortality rates and (2) incidence of thrombo-embolic complications.

Our experience is that 34 of the control group of 84 persons died within six weeks of the onset, giving a mortality of 40.5%. This contrasts with the 16 deaths among 70 persons in the treated series, with a mortality rate of 22.8%. It would appear that by efficient anticoagulant therapy during the first three weeks after the myocardial infarct the mortality rate in the first six weeks may be almost halved. Our experience confirms the American conclusions to which reference has already been made.

When the sexes are considered separately it is apparent that the males show a greater improvement than do the females. The reduction in male mortality rate is of statistical significance, the degree of probability (P) being less than 0.05. In the control group of males the death rate was 33.3%—18 deaths among 54 men. In the treated group, composed of 46 males, 7 died, giving a mortality rate of 15.2% (Fig. 4). This is a striking difference, and, being of statistical significance, we conclude that in males, during the first six weeks after a myocardial infarct, the death rate can be reduced by half. Analysis of the figures for females does not allow similar deductions, largely owing to the smaller number of cases observed. In the control series 16 of the 30 females died, giving a mortality rate of 53.3%; whereas 9 deaths occurred among the 24 females in the treated series, the mortality rate being 37.5%. Such a difference is not of statistical significance.

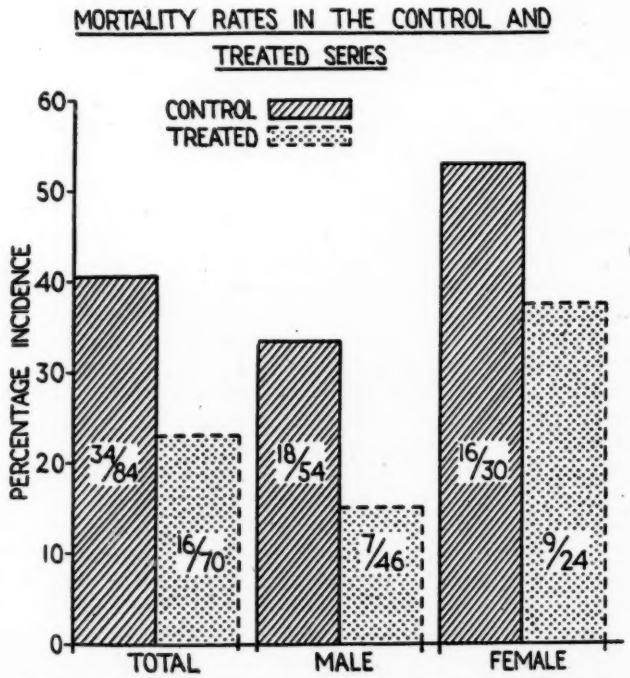

FIG. 4.—Efficient anticoagulant therapy reduces the total mortality rate by half. The difference is statistically significant among men. The smaller experience, based on 30 "control" and 24 "treated" females, does not justify similar conclusions among women.

In estimating the prognosis after myocardial infarction, one factor of great importance is the state of the heart muscle at the time when the acute coronary occlusion was sustained. By using the method of functional grading to which reference has already been made, it becomes apparent that those patients referred for treatment in the hospital who have been in Grade I immediately prior to their coronary occlusion seldom die, provided they survive the immediate effects of the occlusion long enough to be admitted to the ward. In contrast to this, patients in cardiac Grade II B when the infarct is sustained seldom recover. Grade III cases, already seriously handicapped, never recover. Fortunately, the majority of victims fall into the Grade II A capacity, and it is in this grade that every aspect of the case must be carefully considered.

Our patients classified as Grade II A prior to the infarct total 55 in the control group and 40 in the treated group, including 38 and 23 males respectively. The most striking difference is observed in the mortality of these Grade II A males. Among the control group the mortality was 31.6%, whereas among the treated males 1 of 23 died —a mortality of 4.4%. This improvement is of statistical significance, P being almost 0.01. We make no claim for any betterment in the other groups, male or female, but we suggest that when a larger series of some hundred cases is presented for statistical analysis it would be advantageous to have these patients assessed in regard to their functional capacity before the myocardial infarct was sustained. We have proof that it is possible to influence the course of events favourably in regard to males classified in Grade II A. Our figures do not suggest that one particular age group in either sex derives greater benefit than any other age group.

As a further test of the efficacy of anticoagulant therapy, the incidence of thrombo-embolic episodes in the two groups has been analysed (Fig. 5). No fewer than 24 patients (28.6%) in the control series developed thrombo-embolic complications of one kind or another while under observation, and 13 of these died. Ten deaths were the outcome of the thrombo-embolic complication, while in three cases death was unrelated to the complication. On the other hand, 9 (13%) of the 70 patients in the treated group developed thrombo-embolic complications, and of these 4 died. No death followed immediately on any such

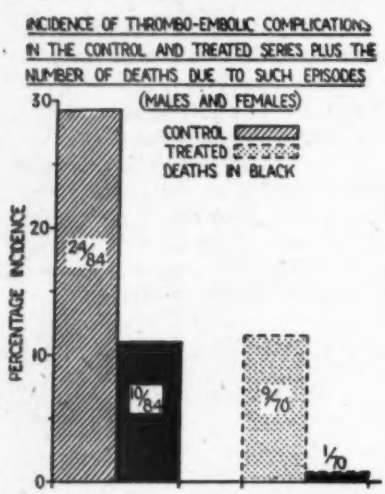

FIG. 5.—The incidence of thrombo-embolic complications was reduced from 28.6% in the "controls" to 13% in the anticoagulant "treated" group. In the "control" group 10 deaths were attributable to these complications, in contrast with one death in the "treated" series.

complication, but in one patient death was related to an embolic incident. The incidence of complications was 13% in the treated group—less than half that observed amongst the controls. Taking the incidence of complications separately between males and females, no significant reduction is observed statistically. However, as the data show no significant difference in the incidence of complications as between males and females, they may reasonably be taken together as one group, and if this is done there is then a significant difference in the incidence of complications between the treated and control groups (P being 0.01). We can therefore confirm the observation of Wright *et al.* (1948) that the incidence of thrombo-embolic complications in myocardial infarction can be reduced by half by the proper use of anticoagulants.

Marple and Wright (1948) have drawn attention to the possible relationship of a lapse in dicoumarol therapy to the occurrence of thrombo-embolic episodes. In this series seven patients sustained thrombo-embolic complications during the first four to five days of treatment, either while heparin was being given or during the 24 hours after the heparin had been stopped. The two episodes occurring at a later date developed in adequately treated males.

Other Complications

Other complications of significance occurring during the period of treatment in hospital were the development of heart failure and the occurrence of arrhythmias. Heart failure developed in 23 cases in each series—an incidence of 27% in the control series and 33% in the treated series. In the control series 17 of the 23 patients died—a death rate of 74%, but in the treated series only 13 died—a death rate of 56.5%. Arrhythmias occurred in seven cases of each series; four deaths occurred in the control group and five in the treated series.

The causes of death in the two series are listed in Table VIII. It will be seen that in the control series death resulted from a variety of causes, while in the treated series the great majority of patients died in heart failure. One patient in each series died suddenly from rupture of the infarcted area. Our necropsy experience in both series is small and unsuited for statistical analysis. In the control series 12 cases came to necropsy. Six showed mural thrombus formation; of these, four had had thrombo-embolic complications. In the treated group there were nine post-mortem examinations. Mural thrombus was found in the ventricles in two patients and thrombo-embolic phenomena were limited to one of these—the first female to be treated—in whom the anticoagulant therapy then employed would now be regarded as inadequate.

TABLE VIII.—*Causes of Death in the Two Series of Patients*

	Control	Treated
Heart failure	7	8
Persistent shock	2	—
Recurrence of myocardial infarct	5	—
Cerebral embolus	3	1
Sudden death	10	7
Coma	1	—
Death within 24 hours of onset	6	—

General Considerations

All the reports in the literature substantiate the claim that anticoagulants are at the present day a remedy of outstanding value in the treatment of coronary thrombosis. By their proper use the death rate and the incidence of thrombo-embolic complications can each be reduced by half—a very substantial contribution to the treatment of this serious disease.

Unfortunately, with the anticoagulants at present available, it is a tedious and difficult form of therapy, depending upon laboratory facilities, a reliable technique, and trustworthy technicians in whose hands is the life of the patient. More laboratory assistants require to be trained for this work so that this particular treatment can be made available to larger sections of the community, even outside the walls of the hospital. Until a domiciliary service can be arranged, the only alternative is to refer such cases of coronary occlusion as are fit to be moved, to those institutions where appropriate laboratory facilities exist for the control of anticoagulant therapy. The practitioner can always begin treatment with heparin in the patient's home, but at present the coumarol compounds cannot be used without daily estimations of prothrombin time. The mortality rate for coronary thrombosis throughout the general population will fall when a larger number of hospital beds are made available for its treatment and when a domiciliary laboratory service provides the practitioner with technical help, without which this particular treatment cannot be undertaken.

No doubt the use of anticoagulants may be simplified in the future. At the present time they are difficult to handle. A painless, inexpensive, slow-acting but reliable substitute for intravenous heparin would be a great advantage. We have been disappointed in depot-heparin and heparin-retard, partly on account of the intense and persistent local pain after the intramuscular injection and partly on account of irregular absorption. "Heparin-Evans" (25,000 units per ml.) has proved more satisfactory when given at eight-hour intervals intramuscularly in doses of 20,000 units. This amount will usually maintain a clotting time in excess of 20 minutes throughout an eight-hour period. We have no personal experience of new synthetic heparin-like substances, such as "paritol," which have the virtue of cheapness and are now under clinical trial (Sorenson *et al.*, 1949). "Tromexan" (Burt, Wright, and Kubik, 1949) possesses certain advantages over dicoumarol in that it comes into action more quickly and is less cumulative. The oral dose being larger, it can be more easily adjusted from day to day. It should be given in divided amounts at 6-hour to 12-hour intervals according to the morning prothrombin-time.

Finally, it is worth emphasizing that there are definite contraindications to dicoumarol and tromexan. In view of the risk of serious haemorrhage, they should not be used in the presence of hepatic or renal disease, or the severer anaemias, pregnancy, or vitamin deficiencies. Any ulcerated surface, particularly of mucous membranes, such as a peptic ulcer or a diverticulitis, may bleed profusely when these drugs are used.

Conclusions

Anticoagulant therapy, suitably controlled by specialized techniques, reduces by one-half the mortality rate during the first six weeks after myocardial infarction. Our experience is that it appears to benefit males to a greater extent than females, particularly men whose myocardial efficiency was only slightly impaired before the acute damage was sustained.

Thrombo-embolic complications are reduced by half, and, when they do occur, fatalities are lessened.

Anticoagulant therapy cannot succeed in the absence of strict attention to the established methods of treatment. It does not shorten the stay in bed.

It should be considered for every sufferer from myocardial infarction. This implies an extension of laboratory facilities for the regulation of treatment and a greater number of hospital beds set aside for this purpose. A scheme for domiciliary laboratory control is desirable if the practitioner is to continue to care for these patients.

For the purposes of this investigation Professor Stanley Davidson, Dr. W. D. D. Small, and Dr. W. A. Alexander have kindly given us access to patients suffering from coronary thrombosis under their immediate charge in the Royal Infirmary. We are also indebted to Mr. George Waugh, F.F.A., of the Scottish Statistical Research Bureau, for help in the statistical analysis of our findings.

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CAPILLARY RESISTANCE AND ADRENOCORTICAL ACTIVITY

BY

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The starting-point of the present investigation was the observation that the resistance of skin capillaries to rupture by negative pressure rises sharply after many types of surgical operation (Scarborough, 1944). It was decided to study the effects on capillary resistance of other types of tissue damage. The variety of such types of damage which produced increased capillary resistance led to the possibility that this rise might be produced by any form of non-specific stress. Positive results were obtained after the application of various forms of stress. Interest was then stimulated by recent work on the physiology of the pituitary – adrenal axis, and it seemed possible that all the conditions which had been investigated were such as would lead to activation of this axis through the release of endogenous adrenaline or through some other pathway as yet unknown. This paper describes the investigations outlined above, leading to the study of the effects of the injection of adrenocorticotrophic hormone (A.C.T.H.) on capillary resistance.

Methods

Capillary resistance has been measured throughout these studies by a negative pressure method. The apparatus (Fig. 1) was the same as that used by

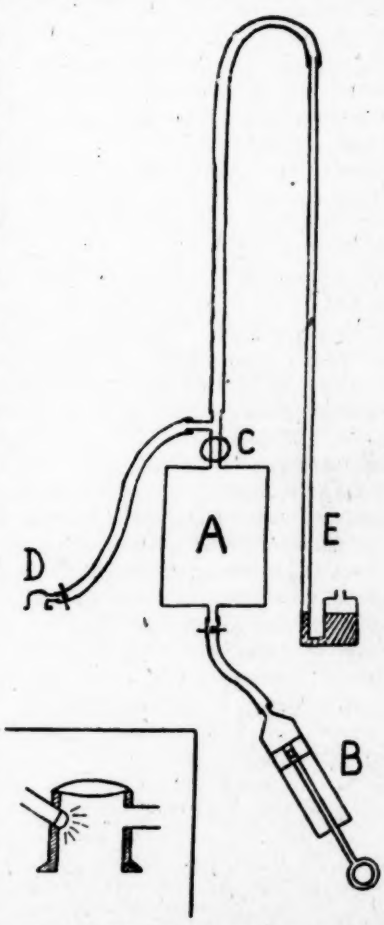

Fig. 1.—Diagram of apparatus used.

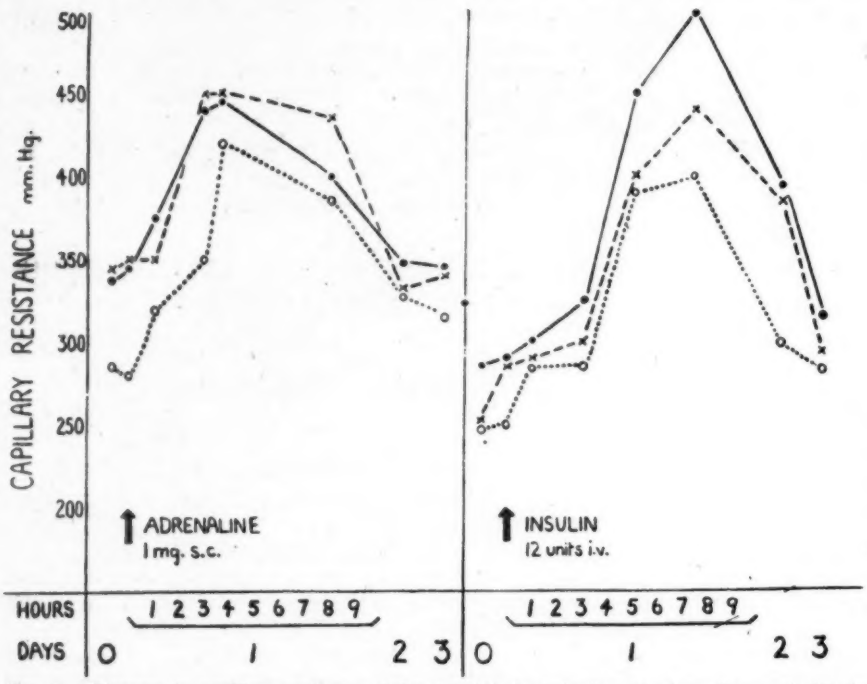

FIG. 2.—Changes in capillary resistance following (*a*) the injection of adrenaline, and (*b*) the production of insulin hypoglycaemia.
×----× Medial elbow region. O.....O Lateral elbow region.
●——● Wrist region.

Scarborough (1941). Negative pressure is created in the reservoir (A) by means of a suction pump (B). The control valve (C) allows suction to be applied to the skin in the test area through the cup (D). The degree of negative pressure is recorded on the mercury manometer (E). The suction cup used has an internal diameter of 20 mm. A lens of ×10 is incorporated in the roof of the cup. Standard illumination is obtained from an endoscope bulb which projects from the wall of the cup and is lit by a 2-volt dry battery.

The principle employed in using this apparatus was the determination of the "critical petechial pressure"—that is, that negative pressure which when applied for 30 seconds would produce one or two petechiae only in the test area. At each estimation three standard areas on the volar aspect of the forearm were tested (Scarborough, 1941), the same arm being used throughout studies on any one patient, and, when recorded daily, readings were taken at approximately the same hour. In order to reduce the number of trial readings at any one estimation, alterations in pressure were usually made at intervals of 500 mm. Hg. It has been found by experience that when any given pressure produces up to but not more than 10 petechiae it is usually unnecessary to make further trial, since a pressure of 50 mm. less will not produce any petechiae. If more than 10 petechiae are produced, then it is necessary to repeat the observation at a lower pressure in an immediately adjacent area. For the purposes of graphing results only, it has been assumed that between the intervals of 50 mm. of pressure the "critical petechial pressure" is proportional to the number of petechiae produced.

With the technique described here the average range of normal capillary resistance is 250 to 350 mm. Hg, but occasional wide variation in normal individuals is encountered within a range of 200 to 450 mm. Hg (Bell, Lazarus, Munro, and Scarborough, 1942).

Factors Influencing Capillary Resistance

Physical Agents—Heat, Cold, and Ultra-violet Light.—The environmental temperature is known to affect capillary resistance. Von Borbély (1930) showed that immersion of the body in a warm bath caused a fall in resistance, while a cold bath gave rise to increased resistance. Rossman (1940–1) showed that heating of the whole body in an inductotherm caused lowering of resistance during the period of heating, followed by a rapid rise to supranormal levels when heating was discontinued. Patients undergoing inductotherm treatment have been studied here. No observations were possible during the period of heating.

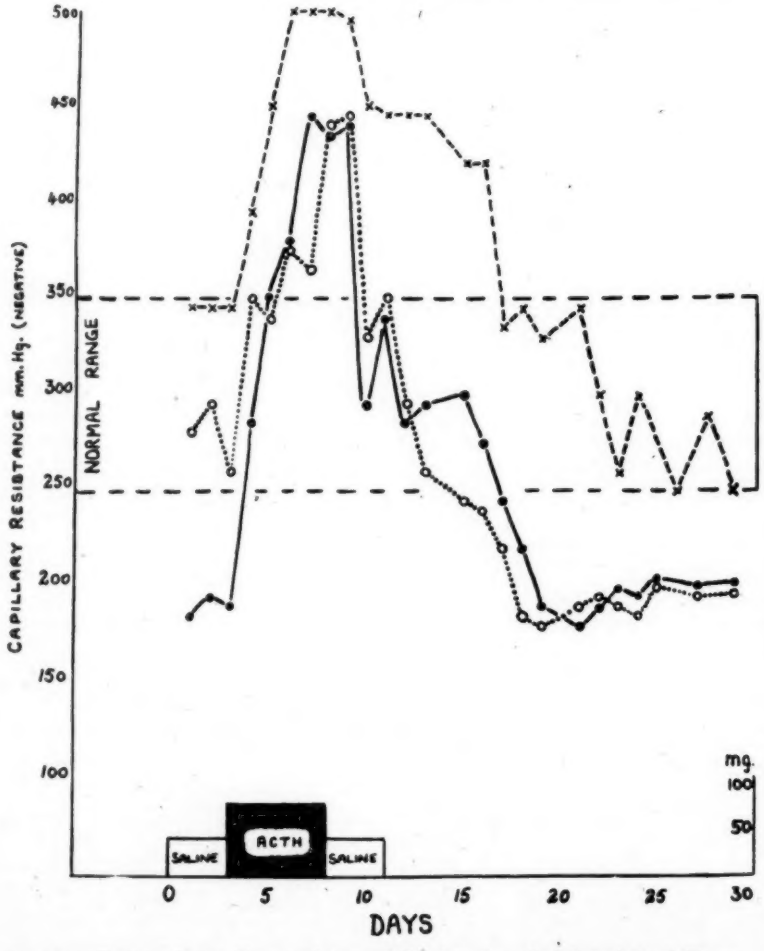

FIG. 3.—Changes in capillary resistance following the administration of 75 mg. A.C.T.H. daily for five days in a case of rheumatoid arthritis.

Table Showing Results in Cases of Rheumatoid Arthritis

Case No.	Area	Range of Readings in Control Period		Readings at 4 hr. after 25 mg. A.C.T.H.		Readings at 8 hr. after 25 mg A.C.T.H.		Maximum Resistance Attained (mm.Hg)	Time to Reach Maximum (hr.)	Time Taken to return to Control Levels (days)	Total Dose of A.C.T.H. (mg.)
		Capillary Resistance (mm.Hg)	Eosins. (c.mm.)	Capillary Resistance (mm.Hg)	Eosins. (c.mm.)	Capillary Resistance (mm.Hg)	Eosins. (c.mm.)				
1	M.E. L.E. W.	240–275 100–250 190–290	141–225	—	52	—	—	400 350 500	72	10	1,050
2	M.E. L.E. W.	325–350 200–250 225–250	166–255	400 250 350	92	360 240 300	114	500 390 400	26	2	75
3	M.E. L.E. W.	340–350 260–300 190–200	152–184	400 375 300	88	350 290 250	109	500 450 450	84	10	375
4	M.E. L.E. W.	320–350 250–300 200–300	66–145	400 400 270	26	450 400 270	50	500 500 420	72	14 (2 areas only)	375
5	M.E. L.E. W.	250–290 200–230 275–290	330–386	300 220 300	120	350 275 380	—	400 350 500	72	12	375
6	M.E. L.E. W.	300–340 250–340 300–340	602–881	380 370 450	266	370 360 400		500 470 500	72	40	375

M.E., medial elbow region. L.E., lateral elbow region. W., wrist region.

but readings taken after removal of the patient from the inductotherm confirmed Rossman's observation that a marked increase in resistance occurs. Franke (1943) reported that exposure to ultra-violet light gave rise to diminished resistance during the period of skin erythema, but that if exposure was continued resistance rose to supranormal levels.

X-ray Irradiation.—Capillary resistance has been measured in patients having radiotherapy for various types of malignant disease. In most cases a marked rise in capillary resistance occurred within three to four days of the beginning of therapy and was maintained during the course. These findings are to be fully described elsewhere (Robson and Court Brown, to be published).

Mitotic Poisons: Nitrogen Mustard.—The intravenous injection of nitrogen mustard in cases of reticulosis has also been found to cause a sharp rise in capillary resistance, sustained for some days after completion of the course of injections.

It seemed possible that, since the agents described above caused some degree of tissue damage, their effects on capillary resistance might be due to the action of histamine or histamine-like substances released by tissue breakdown.

Histamine.—Franke (1943) reported that 1 mg. of histamine injected subcutaneously caused an initial fall in capillary resistance, which was maximal in about 20 minutes, with a return to basic readings in about 45 minutes. He did not record observations beyond that point. Wyss and Gianoli (1946) confirmed these findings. The technique employed in the present investigation was the intravenous infusion of 3 mg. of histamine in a saline drip over a period of one to two hours, usually in cases of rheumatoid arthritis. Capillary resistance was found to fall during the period of infusion of the drug, returning to basic levels in about two hours, and rising thereafter to supranormal levels, the increase being sustained for about 24 hours. The pattern of change in capillary resistance following the infusion of histamine, while bearing some resemblance to the effects of heating and burning, was not the same as that produced by cold, or by surgical operations, irradiation, or mitotic poisons.

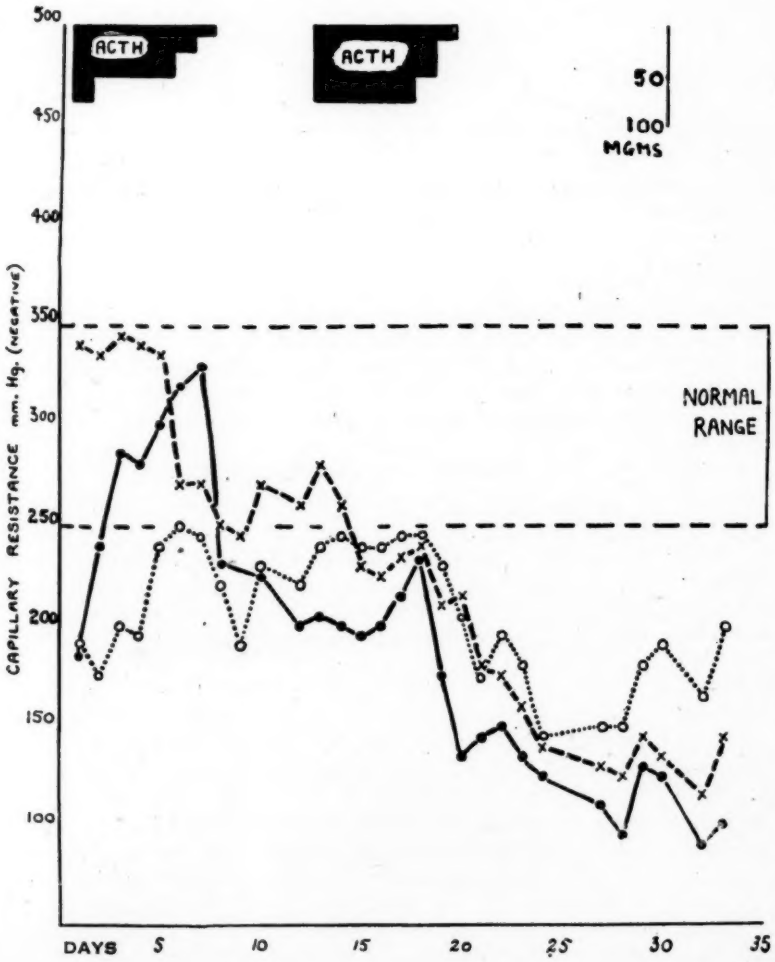

FIG. 4.—Changes in capillary resistance in the case of lupus erythematosus which showed a poor clinical response to A.C.T.H., and in which there was a fatal termination.

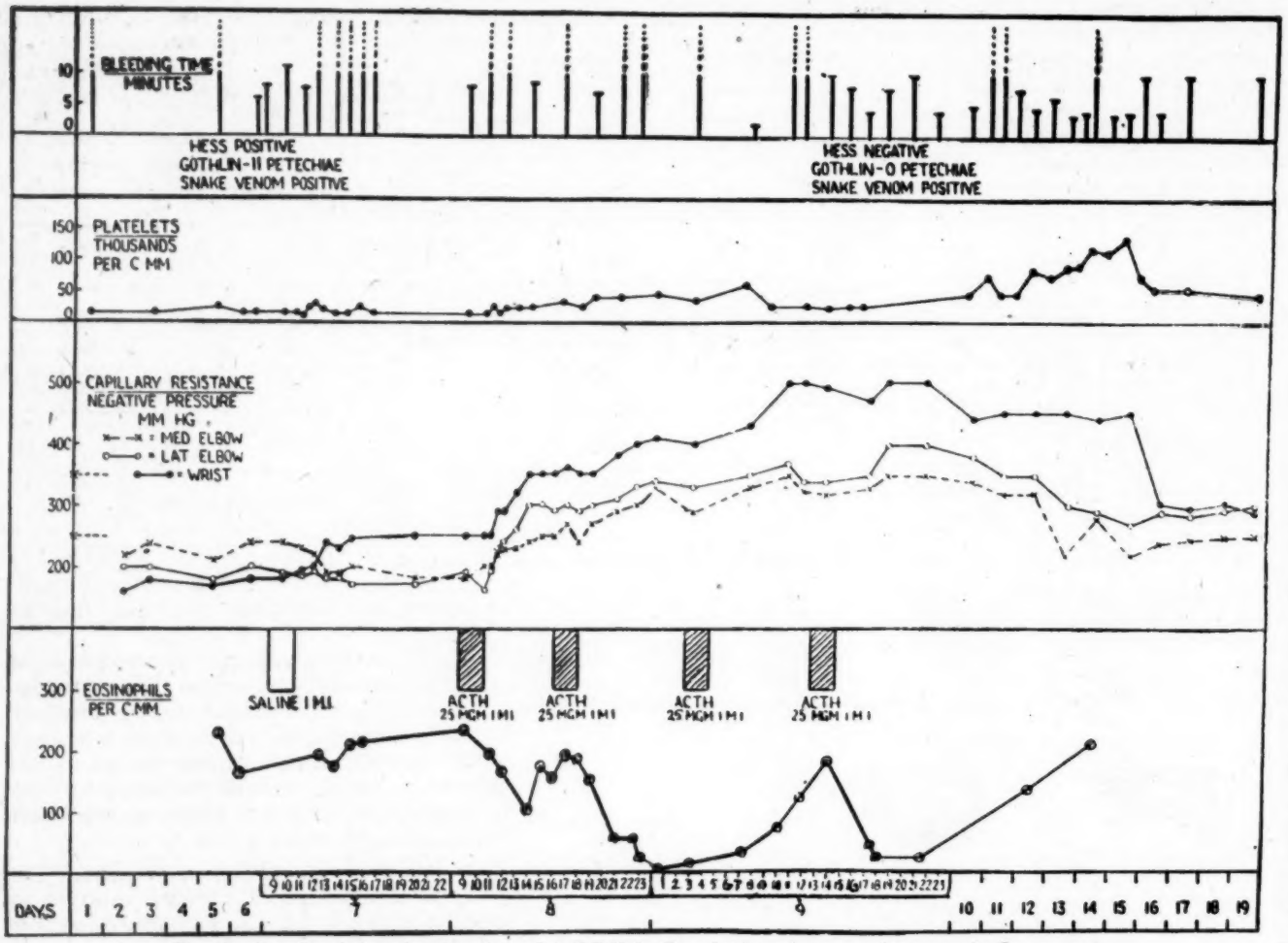

FIG. 5.—Results of the administration of A.C.T.H. in Case A (thrombocytopenic purpura)—first course.

Protein Shock by T.A.B. Vaccine.—Protein shock produced by the injection of T.A.B. vaccine was studied. A fall in resistance was generally recorded during the period of mounting pyrexia, but this was followed by a rapid rise to supranormal levels, reaching a maximum in three to four hours and thereafter slowly returning to the baseline in 36 to 48 hours.

Adrenaline.—It was decided to observe the effects of the injection of adrenaline, since the "alarm reaction" of Cannon is produced by the endogenous release of this substance. Observations were made following the injection of 1 mg. of adrenaline intravenously or 1 to 2 mg. subcutaneously. With either route a rise in capillary resistance has constantly been found, detectable within two hours of the injection, reaching a maximum in four to six hours, and thereafter returning to base levels in 24 to 36 hours. An example is shown in Fig. 2. Similar results have been described by Parrot, Lavollay, and Galmiche (1944) and by Lavollay (1944).

Insulin Hypoglycaemia.—The results obtained by the injection of adrenaline prompted the study of the effects of hypoglycaemia, since this is known to be an effective stimulus to the endogenous release of adrenaline. Observations were made following the injection of soluble insulin, either intravenously in doses of 10 to 15 units, or subcutaneously in doses of 30 to 50 units. One example of the result is shown in Fig. 2. An increase in capillary resistance is usually detectable about one to two hours after the hypoglycaemia is manifest, reaching a maximum in four to six hours, and returning to control levels in about 48 hours.

The observations, when considered in the light of recent work which suggests that adrenaline stimulates the production of A.C.T.H. from the anterior pituitary, led to the idea that increased capillary resistance might be a manifestation of increased adrenocortical activity.

A.C.T.H. and Capillary Resistance

In the course of wider clinical investigations an opportunity arose to study the effects of A.C.T.H. on capillary resistance. Among the cases which have been studied were six examples of rheumatoid arthritis, two of ankylosing spondylitis, two of disseminated lupus erythematosus, and two of idiopathic thrombocytopenic purpura.

Rheumatoid Arthritis

Six patients suffering from this condition have been studied. Fig. 3 illustrates the changes in capillary resistance resulting from the administration of 75 mg. A.C.T.H. daily for five days in one of these cases. The accompanying Table gives brief details of the findings in the six cases. Illustrated are the changes in response to the first dose (25 mg.), the time taken to reach maximum resistance on a dosage of 25 mg. eight-hourly, and the time taken for capillary resistance to return to control levels after the course was completed. It may be seen that a single dose of 25 mg. of A.C.T.H. produced a significant rise in one or more areas within four hours in all except one case, in

which the response was delayed. In this latter case resistance was raised at eight hours after the injection, by which time the others had in general shown a tendency to return to base levels. In all cases, continued administration of A.C.T.H. in doses of 25 mg. eight-hourly resulted in a marked elevation of capillary resistance, reaching a maximum in about 72 hours. Resistance was maintained at this high level for the remainder of the period of administration. When A.C.T.H. was stopped the resistance fell at varying speeds, reaching base levels again in 10 to 14 days. (In Cases 4 and 6 the return was much slower.) No case has been encountered in which a significant fall in eosinophils has not been accompanied by a definite rise in capillary resistance. The extent and speed of the increase in resistance, however, have not necessarily corresponded exactly with the percentage fall in eosinophils. The extent and duration of the increased resistance have borne only a rough correspondence to the clinical effects achieved by the A.C.T.H.

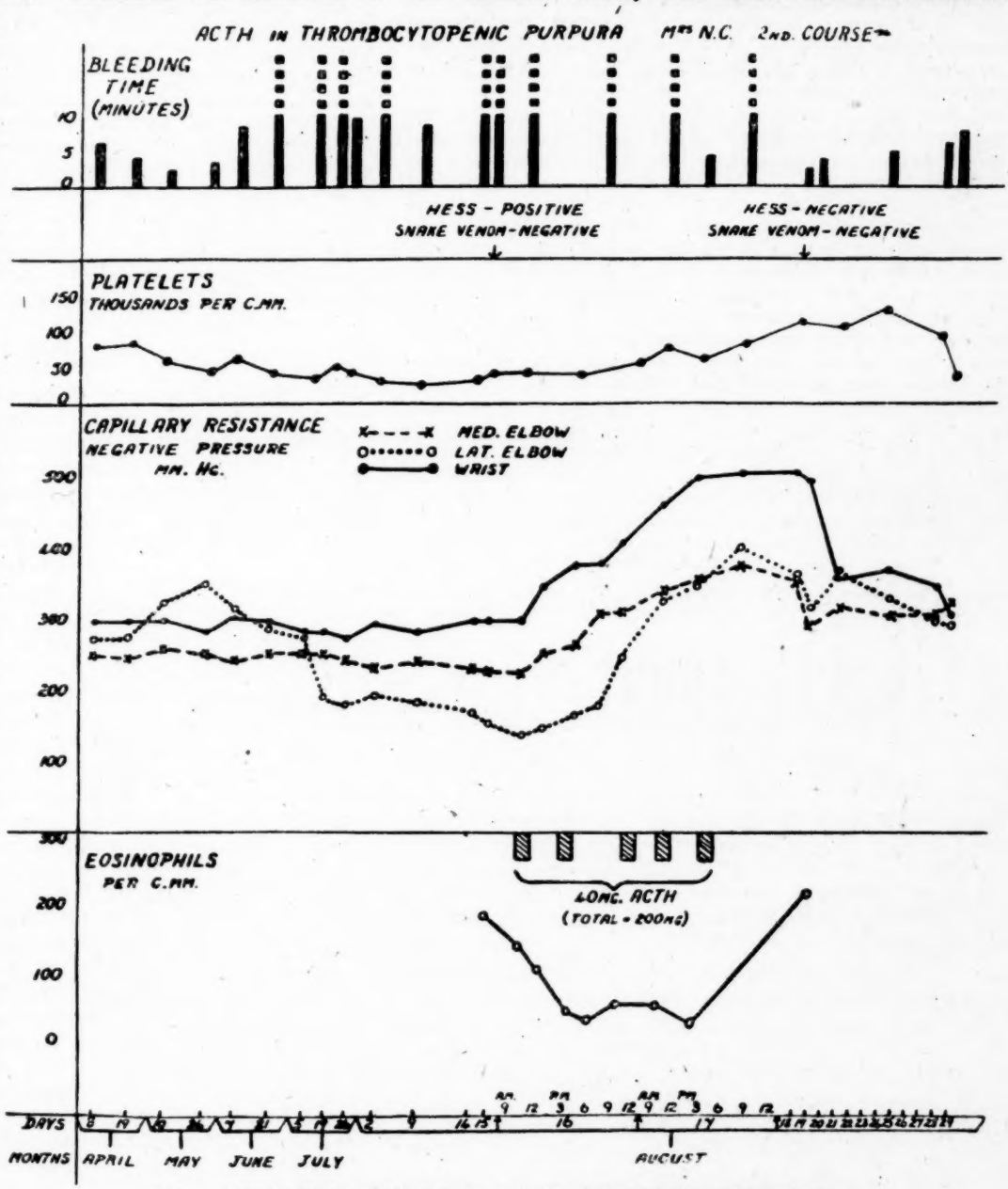

FIG. 6.—Results of the administration of A.C.T.H. in Case A—second course.

Spondylitis Ankylopoletica

Two patients suffering from this condition have been studied. In both a marked increase in capillary resistance was observed following the administration of 75 mg. daily. Resistance reached maximum level in both about 48 hours after the first injection. In both cases resistance fell quickly on completion of the five-day course of A.C.T.H.

Disseminated Lupus Erythematosus

Two patients suffering from this condition have been studied. In both cases capillary resistance was low in the observation period. In one case, eosinophils, which had been entirely absent from the peripheral blood, reappeared before A.C.T.H. was given. A course of A.C.T.H. lasting seven days (total dose 340 mg.) resulted in a marked clinical improvement, a reduction in circulating eosinophils, and a definite increase in capillary resistance. This increase was not long sustained after A.C.T.H. was discontinued, and resistance returned to base levels in four days. Clinical relapse was also quickly evident. The findings in the second case are illustrated in Fig. 4, where it may be seen that the expected increase in resistance did not take place. The patient showed a poor clinical response to A.C.T.H.; her condition steadily deteriorated and death occurred. Eosinophils were absent from the peripheral blood in this case throughout the entire period of observation, before, during, and after the administration of A.C.T.H. At necropsy both adrenals were found to be small, and on section it was noted that lipoid was extremely scanty in the zona fasciculata.

Idiopathic Thrombocytopenic Purpura

Since low capillary resistance is generally regarded as one of the principal features of idiopathic thrombocytopenic purpura, it seemed of interest to ascertain the effect of giving A.C.T.H. in this condition. Reports of two cases follow.

Case A.—A woman aged 33 had had a prolonged episode, starting in 1946 and continuing until spontaneous remission occurred in 1948. During this time she had suffered from ecchymoses and recurrent petechial rashes, but no haemorrhagic incidents had occurred. In December, 1949, on the twelfth day of the puerperium of a normal pregnancy and delivery, ecchymoses and petechiae reappeared. These, together with thrombocytopenia, continued without remission up to the time of the present investigation. The results of the initial administration of 100 mg. of A.C.T.H. in four divided doses are shown in Fig. 5. It may be seen that a definite rise in capillary resistance occurred, reaching a maximum after 75 mg. had been given. When the drug was discontinued, capillary resistance returned slowly towards the control levels in approximately seven days. During the period of elevated resistance the Hess test became negative, but the snake-venom test remained positive; no significant change occurred in platelet counts and the bleeding-time was little altered. It must be noted, however, that a moderate increase in platelets was recorded (maximum about the seventh day) after A.C.T.H. had been given, and that a tendency towards reduction in bleeding-time had become apparent about this period. Clinically, a definite remission resulted, and this persisted for three months, though platelet counts and capillary resistance had returned to low levels. Ecchymoses and petechiae then reappeared and the clinical condition rapidly reverted to that found before the first course of A.C.T.H. As shown in Fig. 6 a second course of A.C.T.H., totalling 200 mg., was given in 40-mg. doses over a period of 48 hours. This resulted in changes similar to those observed previously in capillary resistance, bleeding-time (more definitely reduced on this occasion), and platelets (again a delayed slight increase). Clinical remission has again been produced, although at the time of writing this had been followed for only three weeks. It must be noted that, although the amount of A.C.T.H. given was doubled in the second course, the effects produced were no greater than, if indeed as great as, in the first course.

Case B.—A man aged 32 presented with a history of bruising and petechial haemorrhages for three months, and of bleeding from the gums for one week. The clinical and haematological findings conformed to the diagnosis, and during observation over a period of three weeks there was no sign of remission. As shown in Fig. 7, A.C.T.H. was given in doses of 40 mg. eight-hourly to a total of 340 mg. This resulted in a marked increase in capillary resistance, a definite reduction in bleeding-time, conversion of both the positive-pressure and the snake-venom tests to negative, and a moderate thrombocytosis which was maximal about nine days later. Bleeding from the gums stopped on the second day of A.C.T.H. administration, no further bruises or petechiae appeared, and the patient has remained in complete clinical remission for five weeks. In contrast to Case A, capillary resistance and platelets have remained above the pre-A.C.T.H. levels and the bleeding-time has been maintained within the normal range.

Discussion

The negative-pressure method of estimating capillary resistance has not been so widely employed as have positive-pressure methods such as the Hess, Rumpel-Leede, or Göthlin tests. First suggested by Hecht in 1907, the suction method has been used by such authors as da Silva-Mello (1929, 1930), Mengler (1930), Von Borbély (1930), Adant (1936, 1938), Franke (1943), and Parrot, Lavollay, and Galmiche (1944) on the Continent; by Dalldorf (1933), Dalldorf and Russell (1935), Cutter and Johnson (1935), and Elliott (1938) in America; and by Scarborough (1941, 1943, 1944) and Robson (1949) in this country. The merits and demerits of the method are reviewed by Munro, Lazarus, and Bell (1947).

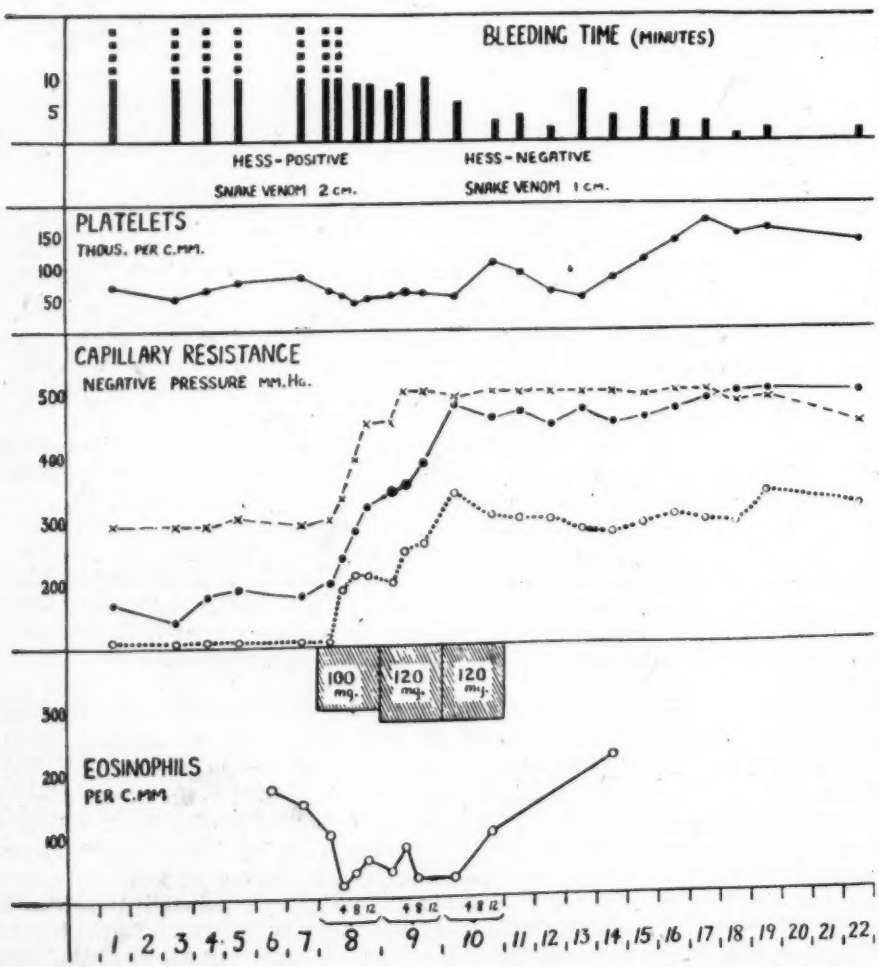

Fig. 7.—Results of the administration of A.C.T.H. in Case B (idiopathic thrombocytopenic purpura).

In the present study, the use of the negative-pressure method has permitted the detection of an increase in capillary resistance, often to markedly supranormal levels, occurring as a result of several different stimuli. These preliminary observations suggest strongly that this rise in resistance is mediated by adrenocortical activity. The number of cases treated with A.C.T.H. is not great, but it seems probable that the extent and duration of the increase in resistance are roughly proportional to the degree of adrenocortical stimulation. In the cases of rheumatoid arthritis, however, the capillary changes did not necessarily reflect accurately the clinical response of the patients to A.C.T.H. In the sixth case of rheumatoid arthritis (see Table), a dramatic clinical remission was produced by A.C.T.H., but this was short-lived. The capillary resistance, however, which was raised to high levels, remained elevated for a considerable period, though complete clinical relapse had occurred. In the fifth case, on the other hand, a prolonged clinical remission was produced by A.C.T.H., but capillary resistance

returned quickly to previous levels after the course was completed. In these six cases of rheumatoid arthritis, and in two cases of ankylosing spondylitis, the correlation between capillary resistance and eosinophil counts was fairly close.

The two cases of disseminated lupus erythematosus provide an instructive comparison. In one case a definite rise in capillary resistance was recorded after the administration of A.C.T.H. in a dosage which resulted in a decided clinical remission and a depression of eosinophils. In the second case, however, no such increase in resistance was recorded, clinical response to A.C.T.H. was poor, and the progressive deterioration was reflected by the falling capillary resistance. Since no eosinophils were found at any time in the peripheral blood in this case, the capillary resistance findings were of great value as an index of the lack of response to A.C.T.H.

The results in the two cases of thrombocytopenic purpura are of interest. It is noteworthy that capillary resistance rises in response to A.C.T.H. in this condition where the capillaries are believed to be abnormal. The moderate increase in platelets which was found to follow this increased resistance occurred at about the same time interval as the maximum thrombocytosis observed after splenectomy. While it would be unwise to draw more than tentative conclusions from such limited experience, definite clinical remission was induced by A.C.T.H. on three occasions in these two cases. Further study of the effects of A.C.T.H. in this and similar conditions would appear to be indicated.

It seems likely that the increase in capillary resistance which has been found to follow the administration of A.C.T.H., adrenaline, and insulin is due to adrenocortical activity. Such activity would account also for the changes in resistance which follow tissue damage and bodily stress. It is suggested that the measurement of capillary resistance provides a fairly simple and rapid method of following the response to A.C.T.H. or to substances which might be expected to have a similar effect.

Summary

It has been observed that an increase in capillary resistance, as measured by a negative-pressure method, occurs after the infliction of various types of tissue damage and after the application of various forms of bodily stress.

The results obtained suggest that this rise in resistance might be due to adrenocortical stimulation by the release of endogenous adrenaline or some similar mechanism.

Patients receiving adrenocorticotrophic hormone (A.C.T.H.) have been studied and the predicted increase in capillary resistance observed. The features of this response are described.

These observations led to the study of the effects of A.C.T.H. in two cases of idiopathic thrombocytopenic purpura; the results are described. Definite clinical remission was induced on three occasions.

It is suggested that capillary resistance estimations may be used in the measurement of the response to stimulation of the adrenal cortex.

Gratitude is expressed to Drs. E. B. French and A. G. S. Hill for much valuable assistance. We wish to thank Professor L. S. P. Davidson for helpful criticism and advice.

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THREE CASES OF SEVERE BURN TREATED WITH CORTISONE*

BY

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In a former study (Crassweller, Farmer, and Franks, 1950), experimental evidence was presented suggesting that the mortality of experimentally burned mice was reduced by the administration of urinary extract fractions such as are known to contain the cortisone-active material. It thus seemed justifiable to consider giving cortisone in the treatment of severe clinical burns. In this paper three cases of severe burn are presented in which routine burn-therapy was supplemented by the administration of cortisone acetate in varying amounts. One case of 70% burn in an adult has done well. The other two patients (both children) died—one, however, 24 days after the burn and following a most promising early clinical response.

In reporting surface area of burns the modification of Berkow's formula (Lund and Browder, 1944) was used. Simple erythema has not been included.

As routine treatment all received occlusive pressure-dressings with light plaster casts. In Case 1 the burned surface was covered with aluminium foil (Brown, Farmer, and Franks, 1948), while in the other two vaselined gauze was used. Fluid requirements were maintained intravenously and by mouth in all cases.

Case 1

A well-nourished male child aged 23 months was admitted to the Hospital for Sick Children, Toronto, on June 8, 1950, in a moribund condition. He had suffered second-degree burns due to scalding, involving approximately 55% of his body-surface, including the legs, thighs, genitalia, and lower two-thirds of the trunk.

Treatment was started within one hour after the accident. To combat severe shock, 250 ml. of plasma was syringed at once into the radial artery. This resulted in an immediate return

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to consciousness. 150 mg. cortisone acetate was administered intramuscularly at this time. In addition to the immediate shock therapy, plasma and normal saline were given intravenously to control haemoconcentration throughout the next few days. The haemoglobin fell on the third day to 7.2 g. per 100 ml., after which 500 ml. of whole blood was given. Daily injections of cortisone were continued to a total of 450 mg. (Fig. 3). In addition, 400,000 units of penicillin were given intramuscularly daily.

Considering his severe burn the child appeared to be doing well clinically, although his urinary output was small and bloody for the first 36 hours. On reduction of protein intake while fluids (glucose and saline) were maintained, his output suddenly increased and his urine became clear. Despite this turn and a normal non-protein nitrogen, he became comatose, with generalized twitchings and mounting fever at the end of the second day. On the third day his condition improved, with return of consciousness and good voluntary oral intake. However, at the end of the fifth day he lapsed into coma and died in respiratory failure with twitchings and hyperpyrexia.

Necropsy failed to reveal any significant findings apart from the burn. The adrenal glands contained adequate sudanophilic material.

Case 2

A girl aged 7 years was admitted to the Hospital for Sick Children, Toronto, on May 28, 1950, showing no evidence of shock other than rapid pulse and thirst. She had suffered flame burns to the extent of 30% of her body surface, involving the dorsum and left side of the trunk, the left arm, and left thigh. About one-third of the damaged area had second-degree burns and the remainder third-degree burns.

Treatment was begun 45 minutes after the accident. Haemoconcentration was controlled by the administration of 5,420 ml. of plasma in the first three days. Oral fluid intake was good throughout, as was also the calorie intake. She received penicillin, 400,000 units daily, beginning on admission.

On the first day the patient was bright and co-operative, but on the second day she began to appear ill, with a rising temperature and increasing pulse and respiratory rates (Fig. 1). Cortisone acetate 100 mg. was administered intramuscularly at this time and continued daily until the eighth day (Fig. 3). The temperature dropped and she remained remarkably well clinically. Dressings were changed on the tenth day. There was complete healing of the second-degree areas. Separation of slough was progressing normally. The dressings were heavily contaminated with *Ps. pyocyanea*. From the eleventh day her condition deteriorated; she had a slowly rising and swinging temperature and showed signs of toxicity suggestive of a septicaemia. Blood cultures were negative. From the twelfth to twenty-second days sulphadiazine and streptomycin were given, with no apparent benefit. Her burned surfaces were examined with the hope of finding a localized focus of infection, but none was found. Granulations were well formed and appeared healthy. She received aureomycin from the twenty-third day. She became comatose and cyanotic, with a rising temperature which terminally reached 107° F. (41.7° C.). Death ensued with respiratory failure on the twenty-fourth day.

On removal of the dressings at necropsy a red macular rash was found over the abdomen and buttocks which had not been present 24 hours previously. The burned surface and dressings were heavily contaminated with *Ps. pyocyanea*, and this organism grew profusely in the culture of heart blood collected at necropsy. Since no other focus of infection was found, it is presumed that she died with a *Ps. pyocyanea* infection.

Case 3

A strong wiry man aged 21 was admitted to Victoria Hospital, London, Ontario, on May 8, 1950, suffering from severe flash burns sustained while working with high-tension wires. There were burns of most of the trunk, face, and neck, most of the left arm, and of the right arm to the elbow. The pubic hair and all the hair of the legs were singed, and there were burns of less intensity over these areas. The overall area of burn, excluding simple erythema, was estimated to be 70%. The total area of third-degree burn was estimated to be 15% of the body surface.

The face and neck were excluded from the occlusive pressure-dressings and were treated with penicillin cream. During the first 90 hours the patient required 24,750 ml. of plasma (Fig. 2) to maintain normal haemoglobin concentration. In addition he received 900 ml. of whole blood and 2,000 ml. of Ringer-lactate solution. He took fluids well by mouth throughout and received high-protein drinks from the second day on.

The patient was seen in consultation on the third day and cortisone therapy was suggested. This phase of the treatment was supervised by Dr. H. McAlpine. Daily cortisone injections were started on the fourth day (Fig. 3) and discontinued on the twenty-seventh day, following a total dose of 2,750 mg. 50,000 units of penicillin were administered intramuscularly every three hours. The patient remained well throughout and showed none of the stigmata of the so-called toxic phase.

Skin grafts were performed on the twenty-sixth, thirty-third, and fortieth days; all of these were successful. Because of the limited undamaged skin available, stamp grafts were used so as to cover a greater area. At the time of writing (seventieth day) the patient is still in hospital awaiting grafting of residual areas.

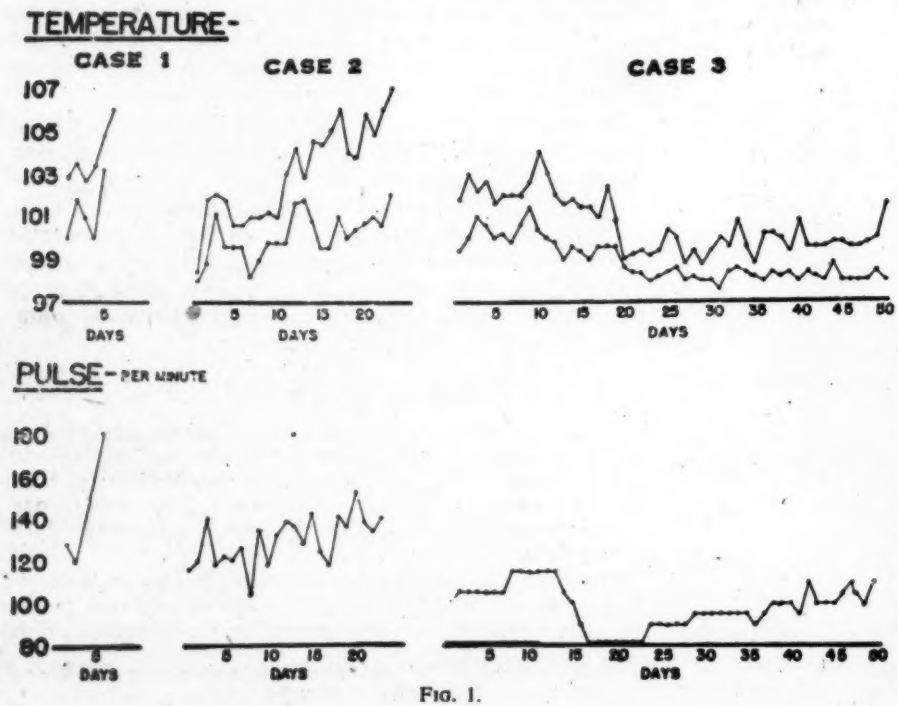

FIG. 1.

Discussion

The first patient (Case 1), according to the tables of mortality probabilities in burns prepared by Bull and Squire (1949), had less than a 40% chance of survival. He received a total of 450 mg. of cortisone over a five-day period. Temperature, pulse, and respiration recordings followed the usual pattern for burns of this severity (Fig. 1). The initial marked depression in the eosinophil count (Fig. 3) was consistent with the severity of the burn (Crassweller, Farmer, and Franks, 1950). With cortisone therapy the initial rise was followed by a return to low levels.

Because of the oliguria, protein restriction seemed indicated and whole-blood transfusion was withheld at this time. Under this treatment an anaemia developed rapidly. The fluid intake, while adequate, was not excessive, so that dilution was not the cause of the low haemoglobin levels. The peripheral-blood smear showed large numbers of microspherocytes, as has been described in severe burns by Brown (1946). The depressed haemoglobin levels may thus have been secondary to haemolysis. Following the return of renal function, 500 ml. of whole-blood transfused on the third day failed to restore the haemoglobin level. Fear of renal complications prevented further transfusion, although it is evident, in retrospect, that transfusions were probably indicated. The anticipated drop in total plasma protein levels did not occur (Fig. 4), and the non-protein nitrogen values remained within normal limits throughout. It is difficult to account for the low total-urinary-nitrogen excretion (Fig. 5) in the face of the usual burn response, coupled with adequate fluid intake and cortisone therapy. As reviewed by Crassweller, Farmer, and Franks (1950), all of these might be expected to result in increased nitrogen excretion. Early hyperglycaemia did not occur, but rising non-fasting blood-sugar levels (Fig. 5), unaccompanied by ketonuria, and in the presence of a relatively constant glucose intake, are perhaps associated with the cortisone therapy. A rising 17-ketosteroid excretion level also suggests a cortisone effect. At necropsy the normal quantity and distribution of sudanophilic material

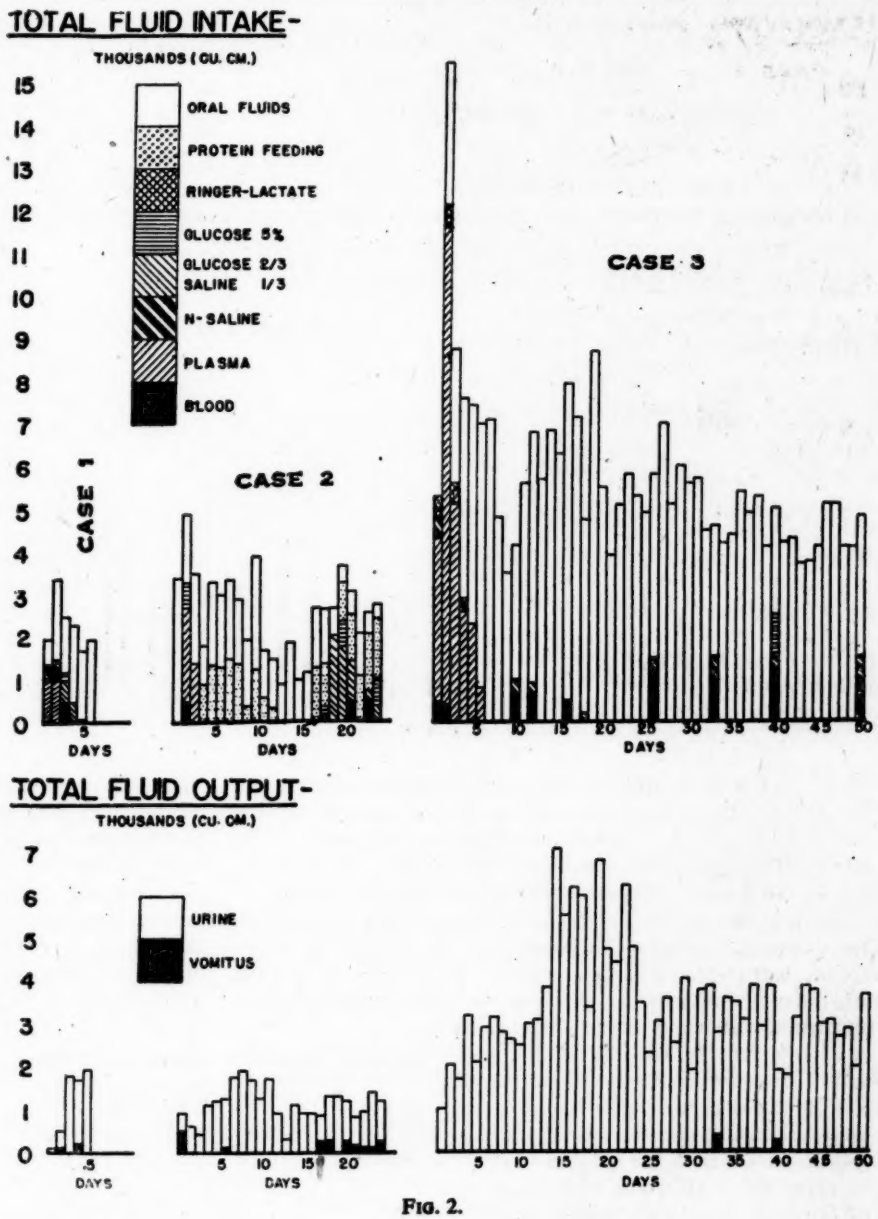

FIG. 2.

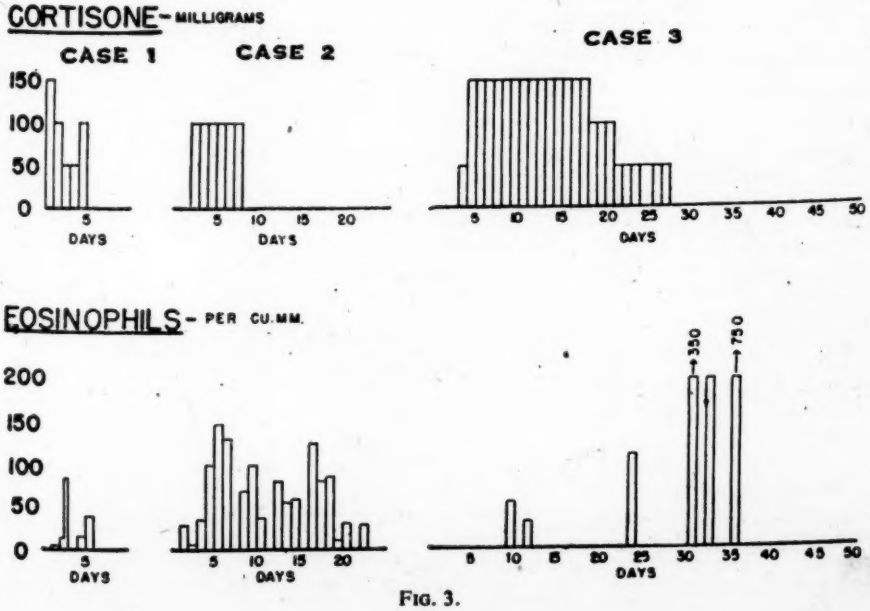

FIG. 3.

found histologically in the adrenal cortices probably indicates that death was not secondary to adrenal exhaustion (Sayers and Sayers, 1949; Cain and Harrison, 1950).

The second case received cortisone 100 mg. daily, beginning on the third day (Fig. 3), following which she improved, and her clinical course was most encouraging. The temperature dropped almost immediately. She was bright and cheerful and displayed a keen appetite. Cortisone was stopped on the eighth day after a total dose of 600 mg. had been given.

After the first change of dressings on the tenth day there followed a slow progressive clinical deterioration. The appetite vanished and it became necessary to feed through a stomach-tube. The temperature

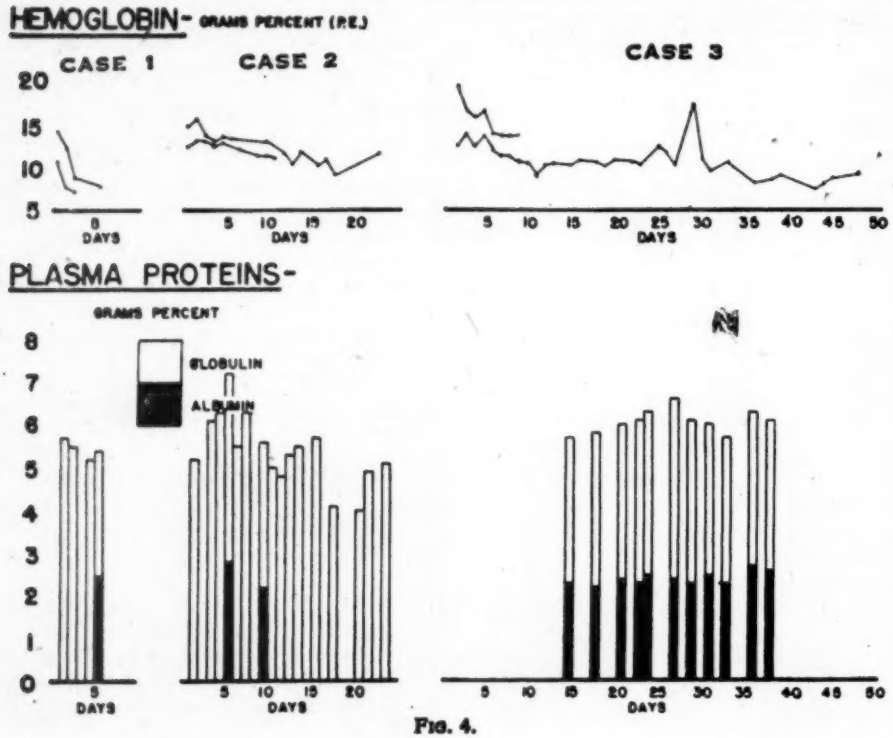

Fig. 4.

assumed a typical septic course and this was reflected in the pulse (Fig. 1) and respirations. A retrograde urinary infection was feared and the catheter was removed. The white blood count reached a level of 32,500 per c.mm. on the eleventh day. Repeated blood cultures were sterile.

During the period of cortisone therapy the eosinophils increased somewhat over the initial depression secondary to the burn (Fig. 3) but remained below the lower limit of normal, suggesting to us at the time that adequate cortisone was being used. However, a steady drop in the daily excretion of 17-ketosteroids in the urine from the third to the tenth day would suggest, from this criterion (Sprague *et al.*, 1950), that the total cortisone dosage was inadequate. A further drop from the eighth to the twelfth day suggests that the production of endogenous corticoids was depressed and remained so during this period. Unfortunately, owing to withdrawal of the catheter, 17-ketosteroid determinations were not available after the tenth day. (Because of the involved nature of the urinary 17-ketosteroid determination (McGill University Clinic modification of the Zimmermann reaction—Hawk *et al.*, 1947), the results were not available to us on a day-to-day basis. Eosinophil counts were therefore followed as the immediate criterion of cortisone therapy (Sayers, 1950). We are now attempting to apply the skin test described by Shuman and Finestone (1950) as a rough measure of corticoids in the circulation.) Continued depression of the eosinophil counts between the eleventh and fifteenth days suggested that the patient was able to respond to the increased stress associated with the onset of infection. Eosinophil counts from the twentieth day onwards led us to believe that the patient was producing adequate corticoids. However, despite the trend of the eosinophil count, post-mortem sections of the adrenal cortices showed a marked decrease in sudanophilic material in the fasciculata and reticularis, and to a smaller extent in the glomerulosa. This suggests adrenal exhaustion (Sayers and Sayers, 1949; Cain and Harrison, 1950) and possibly indicates that 17-ketosteroid excretion estimations are a more reliable guide to adrenal function than the eosinophil count.

The question arises whether or not the administration of cortisone bore any relation to the development of the subsequent infection in the burn. With this in mind, a fractionation of the plasma proteins from a post-mortem sample of heart blood was carried out through the kindness of Dr. A. G. Gournall, Department of Pathological Chemistry, University of Toronto. Using solutions of sodium sulphate of varying percentage as precipitant, the total plasma protein was found to be 4.85 g. per 100 ml. With a 26% solution of sodium sulphate the yield was 2.55 g. of globulin and 2.30 g. of albumin per 100 ml. Using 15% sodium sulphate, the total globulin fraction amounted to only 0.25 g. per 100 ml. Further work is required to determine the significance of this apparently low value. The clinical course in this case, however, was fairly typical of

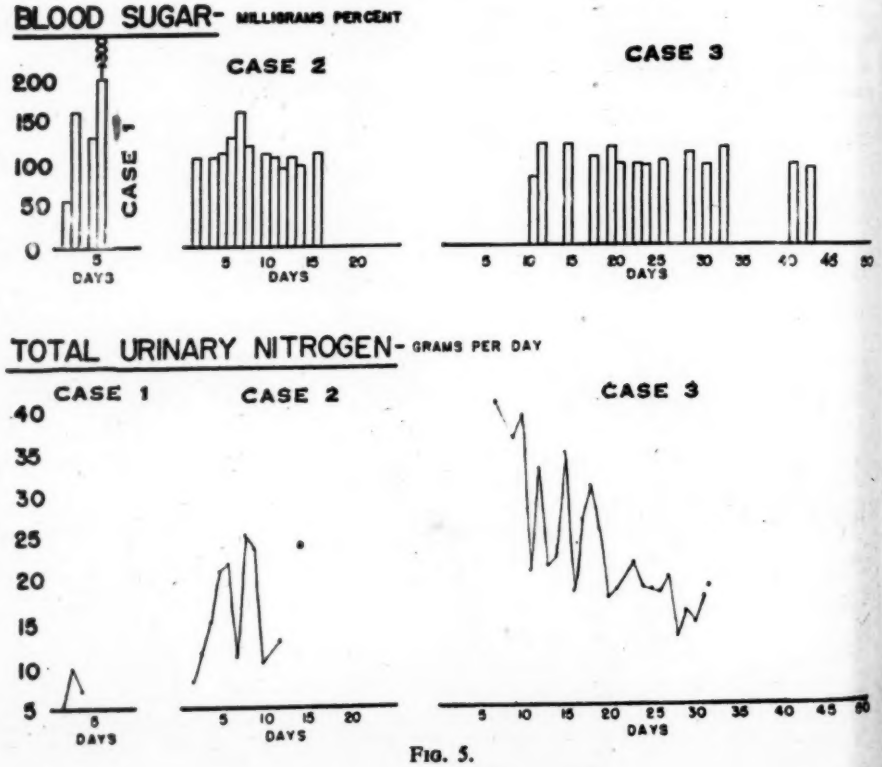

Fig. 5.

Ps. pyocyanea infection as reviewed by Stanley (1947).

According to the tables of mortality probabilities in burns, Case 3 had less than a 5% chance of survival under modern burn therapy. He responded well from the start, even before the administration of cortisone. He did not develop any evidence of pulmonary oedema, despite the fact that on the second day he received 15,500 ml. of fluid (Fig. 2). He did, however, develop marked peripheral oedema, making it necessary by the third day to split the body cast. This oedema probably accounts for the marked positive fluid-balance at this time. Cortisone therapy was begun on the fourth day and continued to the twenty-seventh day. Eosinophil counts were found to be depressed on the tenth, twelfth, and twenty-fourth days (Fig. 3). The cortisone dosage was tapered off on the nineteenth and finally stopped on the twenty-seventh day. The very high counts on the following days may indicate that the endogenous production of corticoids was somewhat depressed. The patient experienced a remarkable state of well-being, almost euphoria, during the period of cortisone administration and after its cessation. Also, he managed a sizeable calorie intake, averaging over 4,000 calories daily and on three occasions reaching 7,000 calories. Although it has been reported (Ragan *et al.*, 1950) that too much cortisone may delay wound-healing, no such difficulty was encountered in this case, despite the fact that the first graft was made during the period of cortisone administration.

Summary

Three cases of severe burn are presented in which routine burn therapy was supplemented by the administration of cortisone acetate.

The first patient, who suffered a 55% burn, died despite cortisone therapy. He had a normal histological distribution of lipoid material in the adrenal cortices at necropsy.

The second patient, who suffered a 30% burn, received cortisone from the third to eighth days, during which period she was remarkably well. Her condition deteriorated clinically after the initial change of burn dressings on the tenth day. She died on the twenty-fourth day, death apparently being due to sepsis. The finding of markedly decreased sudanophilic material in her adrenal cortices suggests adrenal exhaustion at the time of death.

The third patient, who suffered a 70% burn, has done well. He received cortisone from the fourth to twenty-seventh days and displayed a remarkable state of well-being and a keen appetite. This unusual recovery may be related to the cortisone therapy.

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AN UNUSUAL COMPLICATION OF MYANESIN THERAPY IN THE TREATMENT OF TETANUS

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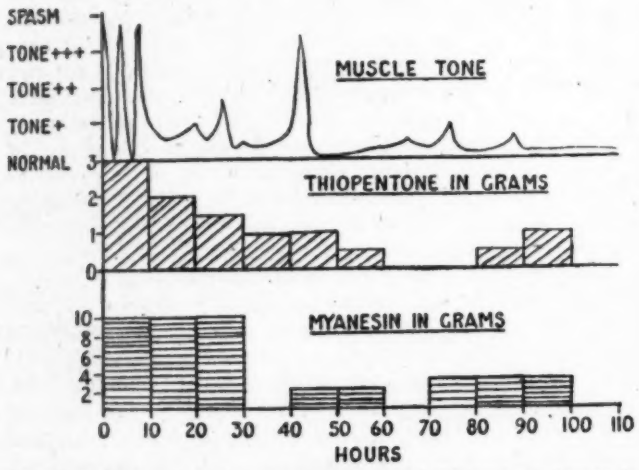
"Myanesin" (α-β-dihydroxy-γ-(2-methylphenoxy)-propane; mephenesin) was introduced into clinical use by Berger and Bradley (1947), and was first used for relief of spasm in two cases of tetanus by Belfrage (1947), with encouraging results. Torrens, Edwards, and Wood (1948) treated a moderately severe case of tetanus with a combination of intramuscular and intravenous injections of myanesin, giving 22 g. in nine days, with considerable benefit to the patient. Davison, Ward, and Pask (1949) also treated two cases. The first case, after a period of treatment with curare and sedatives, was given intermittent intravenous injections of myanesin and recovered. The second was more seriously affected, and myanesin was used from the beginning of treatment. When it was found that a single intravenous injection controlled the spasms for only about 30 minutes, an intravenous glucose-saline drip was set up and myanesin added in varying amounts according to the condition of the patient. After 26½ hours of continuous myanesin treatment haemoglobinuria was observed and the myanesin was discontinued, but the patient immediately relapsed and died from violent spasms two hours later. Macdonald (1949) combined intravenous myanesin with intravenous thiopentone, giving 1–1.5 g. myanesin and 0.5–0.75 g. thiopentone in each 600 ml. of glucose-saline. In 23 days he gave a total of 40 g. myanesin and 32.75 g. sodium thiopentone. No haemoglobinuria occurred, and the patient, a child aged 8, recovered. Godman and Adriani (1949) used the American oral preparation "tolserol" in eight cases of tetanus; all but one of their cases were mild. They found that in doses ranging from 62.5 to 750 mg. in children, and up to 3,500 mg. in adults, it was an extremely satisfactory relaxing agent.

Case Reports

The following are reports of two cases of tetanus in which oral myanesin was used. Rectal thiopentone was also given in the first case.

Case 1.—A man aged 38, an inmate of a colony for mental defectives but of fairly high mental grade, was employed as an agricultural labourer. He gave no history of recent injury. On March 12, 1950, he complained of a painful stiff neck, which was thought to be due to fibrositis; he remained in bed but had no special treatment. The pain increased in severity and spread from the neck to the trunk and legs, and on the morning of March 16 he had a generalized convulsion. He was admitted to hospital, under the care of M. L. N. and J. D. R., at 2.30 p.m. on that day. On examination he was seen to be a well-built muscular man; there was no external injury, and he was fully conscious, flushed, and sweating profusely. There was rigidity of the neck and shoulder muscles with trismus and risus sardonicus. The erector spinae, the anterior abdominal muscles, and all muscles of the legs were in persistent spasm, and clonic contractions of the legs occurred on attempts to flex the knees. The arms were unaffected. No abnormalities were found in the heart, lungs, or central nervous system.

It was decided to treat the patient with a combination of myanesin and rectal thiopentone. At 3.50 p.m. 1 g. of myanesin dissolved in 10 ml. sterile water was given intravenously. Within two or three minutes complete relaxation had occurred, and the change in expression of the patient was most striking as his anxious frown and "risus" relaxed. The patient was given 250,000 units of tetanus antitoxin intramuscularly, and appeared to be comfortable, but by 5 p.m. generalized rigidity had recurred and a further 1 g. myanesin was given intravenously and 2 g. myanesin in tablet form by mouth. Again the intravenous myanesin had a rapid effect, but within half an hour spasms had recurred. At 5.50 p.m. the first dose of 2 g. sodium thiopentone was given per rectum; within 10 minutes the patient had completely relaxed and fallen asleep, but he was disturbed by several sneezing attacks (which are not unknown under light thiopentone narcosis), though these did not precipitate any tetanic spasms. At 8 p.m. there was again generalized rigidity, and the patient was given a further 1 g. myanesin intravenously. He was now ordered 2 g. myanesin by mouth and 0.5 g. sodium thiopentone per rectum, both every two hours. These were given regularly between 11.30 p.m. and 9.30 a.m. the next morning. At 8.50 p.m., about two hours after his third injection of myanesin, he passed



Relationship of muscle tone to myanesin and thiopentone dosage in Case 1.

"port-wine" urine, and the next two specimens of urine, passed at 3.30 a.m. and 4.30 a.m., were also heavily stained. Spectroscopic examination confirmed the presence of haemoglobin, but the specimen passed at 9 a.m. was clear both to the naked eye and on spectroscopy; there was no recurrence of haemoglobinuria.

The following day there was only moderate neck stiffness and the patient was able to speak and swallow without difficulty; he had, however, developed a cough with purulent sputum and there were scattered rales and rhonchi on both sides of the chest. The same dosage of myanesin and rectal thiopentone was continued, but the myanesin elixir was substituted for the tablets. During the day there were only two spasms, both affecting the right leg. The chest condition worsened. Through a misunderstanding the myanesin was omitted during the second night in hospital, though three doses of rectal thiopentone were given. At 7.30 a.m. on the third day the patient had a severe generalized spasm with opisthotonos. Rectal thiopentone was given, followed by oral myanesin, and complete relaxation was obtained within 10 minutes. After this there was no return of major spasms, though rigidity of the neck and abdominal muscles recurred from time to time; this was easily controlled by oral myanesin. The accompanying Graph shows the time-relationship between the spasms and muscular rigidity and the dosage of myanesin and sodium thiopentone.

In spite of decreased dosage of sedatives, the chest condition deteriorated rapidly and the patient died on the evening of his fifth day in hospital. The total dosage of myanesin was 3 g. intravenously and 40 g. by mouth. Altogether 11 g. sodium thiopentone was given per rectum.

At necropsy the body was reported to be that of a well-nourished male. A healing abrasion was present over the left scapula, and there were several splinters in the hands—one 4 mm. long with a surrounding inflammatory reaction and deeply embedded. Anaerobic cultures from this splinter were negative for *Cl. tetani*. No abnormalities were noted in the heart, the central nervous system, or the alimentary system. The lungs showed suppurative bronchitis with early hypostatic pneumonia. The kidneys showed some evidence of old-standing chronic nephritis; otherwise the urinary tract was normal.

Case 2.—A man aged 45 was admitted under the care of G. R. R. on June 7, 1950, at 8.45 p.m. Six days previously while pushing a wooden tomato-stake into the ground he drove a splinter into his left antecubital fossa. He immediately boiled a pair of forceps, pulled out the splinter, dressed the small puncture wound with "dettol," and applied a bandage. Four days later, in the morning, while driving his bus, his back became stiff. The following day, 36 hours before admission, he noticed that his "gums were stiff"; there was some difficulty in chewing. On the day of admission he complained that while walking "something seems to run up and down my spine, and every now and then everything seems to stiffen up—throat, jaws, and back." For the last 12 hours he had been unable to swallow anything.

He was a well-built muscular man, alert and euphoric. He was lying quietly on his back with a stiff neck. There was no neck retraction. His spine was rigid and he was unable to sit up. He was edentulous and could separate his gums by only ¼ in. (1.58 cm.). There were no other abnormal signs, except for the presence of a small unhealed puncture-wound in the left antecubital fossa which appeared moist and unhealthy. There was no lymphangitis nor were there palpable lymph nodes.

A diagnosis of tetanus was made and treatment instituted as follows: Antitetanic serum, 100,000 units intravenously and 50,000 units intramuscularly, was given and sodium penicillin, 250,000 units six-hourly, begun. Myanesin, 1 g. in 20 ml. distilled water, was then given intravenously at 11.10 p.m. Within 30 seconds the patient smiled, said he had not felt so well for days, and asked for a drink. He sat up in bed and could bend his neck so that his chin almost reached his chest. His trismus disappeared and he could separate his gums by about 1¼ in. (3.75 cm.). He was then given 2 g. of myanesin in 2 oz. (57 ml.) of the elixir by mouth. He took one sip and complained of a burning sensation in the mouth; the elixir was therefore diluted with an equal quantity of water. He still found it rather hot and sipped it slowly. At the fifth sip he clutched his throat, had a violent attack of coughing, and, with his eyes bulging and tears streaming down his cheeks, rapidly became greatly distressed. The paroxysm lasted about two minutes, and on his recovery he said, "It went down the wrong way, doctor." It was noticed that though he had stopped coughing a rattling noise was coming from the trachea. From then on until his death signs in the chest became progressively more prominent. The patient was encouraged to finish his elixir and was given a further 2 oz. half an hour later. With this second dose there was again a paroxysm of coughing. With neither of these paroxysms was there any return of spasticity. At 12.30 a.m. he was taken to the theatre and his wound excised under nitrous oxide, oxygen, and "trilene" anaesthesia. A swab from the wound failed to yield any *Cl. tetani* on culture. Unfortunately the tissue removed was not examined. More myanesin was then given—2 oz. of the elixir at 2 a.m. and 4 a.m., the latter dose being swallowed slowly and with difficulty. At 5.15 a.m. abdominal cramps and dysphagia necessitated a further 1 g. myanesin in 20 ml. distilled water intravenously. Relaxation was immediate, and at 6 a.m. the patient managed to drink a further 2 oz. of the elixir. At 9 a.m. he objected to the elixir, so crushed tablets (2 g.) were substituted. At 9.15 a.m. he tried to cough up some mucus, became intensely cyanosed, and had a generalized clonic convulsion with loss of consciousness. Mucus was sucked from his pharynx, and after artificial respiration and the administration of oxygen with 5% carbon dioxide he

recovered. Postural drainage then produced a good deal of thick mucopus. Numerous rales could now be heard at both bases and in the left axilla. At this stage lumbar puncture yielded normal fluid. The urine was clear. At 11.15 a.m. a further 2 g. crushed tablets of myanesin was prescribed, but he was unable to swallow the powder, and it was noticed that some of the previous dose was still adhering to the tongue and the pillars of the fauces. It was therefore decided to give 1 g. myanesin intravenously and then pass a stomach tube. However, every effort to pass a Ryle's tube or an oesophageal catheter (12E) resulted only in tracheal intubation. It is noteworthy that this caused no distress or cough. The attempt was then abandoned. A further 1 g. myanesin was given intravenously at 3 p.m., and soluble phenobarbitone 3 gr. (0.2 g.) intramuscularly as he had not slept since admission. A quarter of an hour later he again started to cough, became cyanosed, and had clonic convulsions. Resuscitation failed, and he died.

At necropsy the brain was intensely congested, but apart from this appeared normal. The trachea and bronchi contained a moderate amount of mucopurulent fluid, and there was marked congestion of both lungs with bronchopneumonia at the bases. The heart showed no macroscopic abnormality. The liver was congested. The spleen and kidneys appeared normal.

Discussion

Cole and Spooner (1935) describe four degrees of severity of tetanus. In the second degree there is generalized tonic rigidity; in the third the tonic rigidity passes on to the stage of reflex spasms. Our Case 1 corresponds to the third category, and according to those authors this bears a poor prognosis. Case 2 corresponds to the second category, in which the prognosis is better; but the short incubation period in this case indicates a severe attack. Both patients responded extremely well to intravenous myanesin, and in the first case the oral myanesin was of considerable value in controlling spasm.

In the first patient it appeared that during the last three days of his illness the tetanic symptoms were under control and required only small doses of antispasmodics and sedative, but he had already developed signs of bronchitis by the second day in hospital, and it seems likely that he was too heavily sedated during his first 15 hours of treatment. It is not thought that the myanesin was responsible for the development of the chest complication, as even when given intravenously it did not depress respiration. The two drugs appeared to have a synergistic action, as when both drugs were given the patient was easily controlled; but when, as during the second night in hospital, the myanesin was withheld, a very violent spasm occurred (see Graph). Both drugs were easily administered. The sodium thiopentone was given rectally in 10% solution. The patient could swallow freely, or the elixir could easily have been given by tube.

With the second patient, although the elixir was diluted with an equal quantity of water after the initial sip, it still burnt his throat and he was unable to swallow it as a draught. After a few minutes he found that the solution no longer burnt him. This we now believe to have been due to the local analgesic action of the elixir on the pharynx. It was at this stage that there was the first violent fit of coughing: quite clearly some of the elixir entered the trachea. From this point a rapidly progressive purulent bronchitis developed. With the second dose further elixir was inhaled. The substitution of powdered tablets for the elixir, coming at a time when swallowing was again difficult, resulted in the powder adhering to the tongue and the mucous membrane of the mouth and fauces, where it exerted its local analgesic action. It was this analgesia that accounted for the stomach tube passing straight into the trachea at every attempt without producing any cough or distress. It is probable that during this period saliva containing dissolved and undissolved myanesin was trickling down the trachea. This would account for the very rapid development of the severe bronchitis in a man with no previous chest history who was receiving penicillin and was nursed sitting upright throughout his illness.

The asphyxial attacks seemed to be due to mucopus being coughed up and accumulating at the back of the pharynx. The presence or absence of laryngeal spasm could not be determined, but it was noticed that there was no trismus or neck stiffness. The convulsions followed the intense cyanosis and were presumably anoxaemic in nature rather than tetanic.

Myanesin has two properties. It causes muscle relaxation by an action on the central nervous system: this may be a depressant action on the reflex excitability of the spinal cord. Its second property, on which no emphasis has been placed in the literature to date, is its local analgesic action. This we believe to be important, and indeed consider it to be directly responsible for the fatal outcome in Case 2. In view of this local analgesic property we feel that myanesin should not be given by mouth to patients with tetanus, in which dysphagia is a common occurrence.

A suggested scheme of treatment would be to begin with an intravenous injection of myanesin, 1 g. in 20 ml. distilled water. This should cause relaxation and enable a Ryle's tube to be passed into the stomach. Two ounces of myanesin elixir could then be given via the tube and repeated half an hour later. In the early stages two-hourly doses of 2 oz. (57 ml.) myanesin elixir by stomach tube would probably be needed, and it might be necessary also to give 0.5 g. thiopentone per rectum. Later the dose of myanesin could cautiously be reduced and the time interval between doses increased. It is felt that the intravenous preparation is of considerable value in the rapid control of severe spasms. The risk of haemoglobinuria after oral myanesin appears to be remote, as it did not recur in our patient after a further 40 g. by mouth, nor did Godman and Adriani (1949) report it in any of their eight cases. In those cases in which oral intubation is difficult or poorly tolerated myanesin could be given in doses of 1 g. intramuscularly.

It is stressed that myanesin should be used solely as an adjunct to treatment with antitetanic serum, penicillin, and local wound excision. The patient should be sedated as little as possible and nursed in the sitting position.

Summary and Conclusions

Two fatal cases of tetanus treated with myanesin are described. The first case also received rectal thiopentone.

Investigation showed that myanesin, given intravenously and orally, is a useful relaxant and controls tetanic spasms satisfactorily; and that when used in therapeutic doses it does not depress respiration.

Myanesin has a local analgesic action and should never be given in powder form by mouth. The elixir should not be given when there is dysphagia. When administered intravenously the risk of haemoglobinuria is diminished by adequate dilution, and may be ignored.

In the second case death occurred from lung complications due to the inhalation of myanesin elixir.

We wish to thank Dr. A. Lisle Punch for permission to treat and publish the first case.

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CASE OF TETANUS TREATED WITH DECAMETHONIUM IODIDE

BY

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In the treatment of tetanus the efficacy of muscle relaxants in preventing exhaustion of the patient from excessive muscular activity has already been shown. Curare has been used by several workers (Hoche, 1894; Cole, 1934; Mitchell, 1935; West, 1936; Cullen and Quinn, 1943; Adriani and Ochsner, 1947; Ory and Grossman, 1948); more recently the use of "myanesin" (mephenesin) has been reported (Belfrage, 1947; Davison, 1949; Davison *et al.*, 1949). It may be of interest to report a case of tetanus in which the relaxant used was the much discussed bistrimethylammonium decane di-iodide (decamethonium iodide, or C10). There were four main reasons for the choice of C10: (1) Both D-tubocurarine chloride and "flaxedil" had been tried by the physicians in charge of the case, with the production of marked respiratory depression and profuse salivation. (2) Myanesin was considered, but, in view of its tendency to produce haemoglobinuria, was rejected. (3) Experience with C10 in anaesthesia has shown that adequate relaxation of the larger skeletal muscles could be achieved without profoundly depressing respiration, and without relaxing the pharyngeal muscles. (4) C10 has less power to liberate histamine than D-tubocurarine chloride and therefore to produce bronchospasm.

Case Report

A girl aged 19 was admitted to the Belfast City Hospital on April 28, 1950, with a history of trismus and severe backache for four days, and opisthotonos and spasms, with very severe pain since the previous day. Two weeks previously she had got a wooden splinter under her finger-nail.

On examination she was seen to be a healthy, well-nourished girl, with a typical risus sardonicus, moderate opisthotonos, and marked trismus—being unable to put out her tongue, and spasms lasting 20 seconds occurring every two minutes; between spasms the muscles were rigid. A clinical diagnosis of tetanus was made (unfortunately the splinter was thrown out with the soiled dressings and a piece of loose nail which separated), and the patient was treated with massive intravenous doses of A.T.S., penicillin, and sedatives. This treatment was successful at first, but spasms returned as soon as the effect of sedation lightened and she became restless.

On the third day small injections of curare in oil were tried, with no effect. Intravenous D-tubocurarine chloride was then tried in 10-mg. doses, and flaxedil in 40-mg. doses, both achieving profound relaxation with respiratory depression for periods of about 30 minutes, after which rigidity and spasms returned as before. The pulse rate and temperature remained high, and the patient's general condition was poor. The physicians in charge of the case decided to seek my opinion as an anaesthetist, and the following treatment was carried out.

On examination the patient was distressed, crying out with the pain of the spasms, flushed, and sweating profusely, and the muscles of the trunk and limbs were rigid. It was decided to try the effect of C10. At 11.45 a.m. on May 2 a slow intravenous injection of C10 was started, 1 mg. at a time. During half an hour 5 mg. was given, producing some relaxation and no respiratory depression. A further 3 mg. was given over the next 15 minutes. The respirations became shallow and cyanosis developed. The injection was stopped and the patient was turned on to her side with her head over the side of the bed, and oxygen was administered by mask. The pharynx filled with sticky mucus, which was periodically swabbed out. She remained unconscious for one hour. The breathing then became noticeably deeper, and she opened her eyes. Fifteen minutes later she was sitting propped up, coughing, and blowing out mucus. After another 15 minutes 1 mg. of C10 was given intramuscularly with 50 mg. of pethidine intravenously and 50 mg. intramuscularly. She was then put in an oxygen tent at 2 p.m.

Small intramuscular doses of C10 and pethidine were given at 7 p.m. and the patient remained comfortable until 9.45 p.m., apart from slight tremors which were seen mainly on effort. Spasms then returned, and a further intravenous injection of 2 mg. of C10 with 50 mg. of pethidine was given, followed by the same dose intramuscularly. An extract from the notes summarizes the effect of these injections. "10 p.m.: Patient restless, crying out, tearful, and frightened. After injection: Quiet, rational, grateful."

In 48 hours 50 mg. of C10 and 950 mg. of pethidine were given. Spasms returned as the effect of the injections wore off, but were easily controlled, and the patient's general condition was much improved. On the evening of the third day of treatment her temperature rose and coarse crepitations were heard at the left lung base. C10 was withheld and a course of streptomycin started. She was encouraged to cough, and postural drainage, with deep percussion, was instituted. With the energetic co-operation of patient and nursing staff the chest was cleared in less than 24 hours. During this time it was necessary to increase the dosage of pethidine to 600 mg. a day. Pain was fairly well controlled, but spasms were troublesome and sleep was disturbed.

After this incident 1/100 gr. (0.65 mg.) of atropine was given six-hourly to cut down secretions. Treatment with C10 was restarted and continued for a further five days, dosage and frequency being judged by the response of the patient. The usual requirement was 2–3 mg. every four to five hours. It was found that, even with the large amounts of pethidine being given, a soporific was necessary at night. The chest remained clear, the spasms became less frequent and less severe, and her general condition improved.

On the evening of the tenth day of the treatment (the fourteenth day since admission) it was noticed that the occasional spasms now coincided with the appearance of the medical attendants. We came to the conclusion that the patient had probably

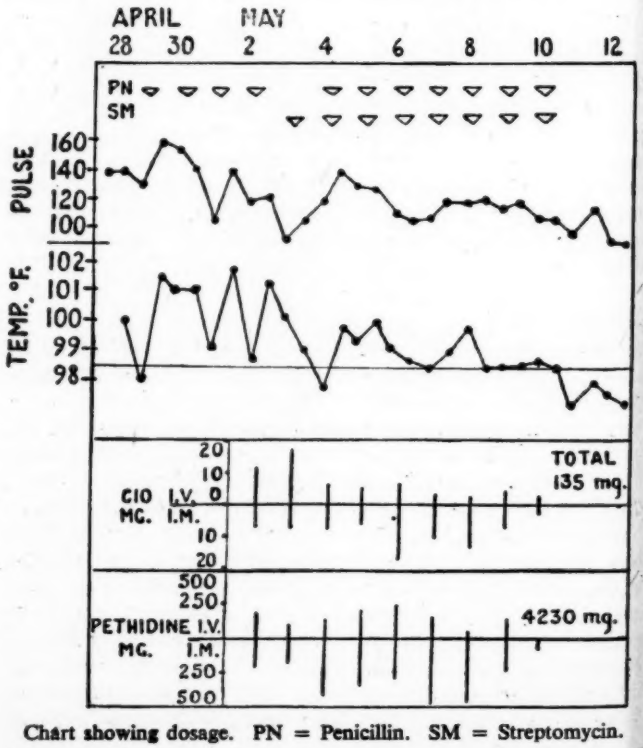

Chart showing dosage. PN = Penicillin. SM = Streptomycin.

developed a mild addiction to pethidine. Paraldehyde, 4 mg., was given intramuscularly. This raised a storm of tearful protest, but the patient slept soundly and no further spasms were seen. On May 15 she was up in a chair, and on May 23 walked with assistance. The muscles were still sore and stiff, but recovery was helped by physiotherapy. She was discharged on June 8.

The total dose of C10 was 135 mg., representing a daily average of 15 mg., and of pethidine 4,230 mg., with a daily average of 470 mg. The distribution is shown in the Chart.

Discussion

The treatment of tetanus with relaxants is not curative. It is still necessary to give A.T.S. and penicillin in massive doses and to build up the patient's general resistance. The experience gained in the treatment of this case, together with a study of the literature, enables certain general principles to be stated.

Sleep.—Even when painful spasms are abolished there may be a fair amount of residual pain from aching and torn muscles, so that an analgesic must be prescribed as well as sedatives to ensure sufficient sleep.

Secretions.—It is futile to abolish the spasms of tetanus, only to let the patient drown in his own secretions. Atropine is useful to cut down secretion. The cough reflex must not be dulled by sedatives, and the patient must be encouraged to cough. If necessary, curarization must be lessened to enable the patient to cough.

Oxygen.—Adequate oxygenation must be ensured. Anoxaemia increases the permeability of the capillaries in the lungs, allowing fluid to escape into the alveoli. If respiratory depression is present, oxygen must be administered. It is suggested that if adequate ventilation cannot be maintained by other means the patient might be nursed in an iron lung.

Nutrition.—Feeding presents no difficulty, since with C10 the patient is usually able to swallow. If, however, the effort proves exhausting, a fine plastic tube, as recommended by Bull *et al.* (1949), can be passed into the stomach with remarkable ease.

Fluids.—Fluid intake and output should be checked and an adequate balance maintained. If the temperature is high, much fluid may be lost by sweating and through the lungs. Haemoconcentration should be watched for by repeated haemoglobin estimations. Urinary chlorides should be estimated and any deficiency made good.

There should always be available a supply of oxygen, with a facepiece and reservoir bag, a mouth gag, tongue forceps, a sucker, and a supply of gauze wipes, a laryngoscope, and endotracheal tubes.

Comparison with Other Relaxants

The causes of failure with curare in the treatment of tetanus are the inadequate margin between the lissive dose and that causing respiratory paralysis, bronchial spasm, and accumulation of secretions.

Myanesin seems to have none of the disadvantages of curare. It has, however, two of its own: a tendency to cause venous thrombosis at the site of injection, and the production of haemoglobinuria. Davison (1949) makes out a very good case for the use of this drug in tetanus. He points out that proof of haemoglobinuria is lacking, since the breakdown products of the drug may produce a positive reaction to the benzidine and guaiac tests, and, further, that in no case has the so-called haemoglobinuria been shown to have any adverse effect on the patient.

C10 has the disadvantages of neither curare nor myanesin. In the above case, on only one occasion was respiration depressed to such an extent as to require inflation of the lungs with oxygen. This occurred with a very large dose —9 mg.—given initially. It is of interest to note that this amount was required to produce relaxation after two intravenous injections of 5 mg. of D-tubocurarine chloride had been given 50 minutes and 1 hour previously. This confirms the experimental finding of Paton and Zaimis (1948) that, although the potency of D-tubocurarine is not affected by the previous administration of C10, twice as much C10 is required after a previous dose of D-tubocurarine. Subsequently, the dosage averaged 2–4 mg. at three- to four-hourly intervals. On one occasion 5 mg. was given, but this dose paralysed the intercostals, and, though no cyanosis was seen, the patient was put in the oxygen tent.

West (1936) expressed the opinion that the development of bronchial spasm was a very real danger in the use of curare. The occurrence of this complication is probably less likely with the pure D-tubocurarine chloride now available, but even with this material it is still seen fairly often. Paton and Zaimis (1948) found that the power of C10 to liberate histamine was one-quarter that of an equivalent dose of D-tubocurarine. This leaves an adequate margin of safety.

Accumulation of mucus was seen after the first dose of C10, and on the third day there were signs of fluid at the base of the left lung. Otherwise there was no trouble with excessive secretion. Coughing and swallowing were possible throughout the treatment. I feel that the choice of analgesic helped to achieve this result.

Pethidine is structurally related to atropine, and has mild atropine-like properties (Batterman and Himmelsbach, 1943). In addition to its analgesic and sedative action, it has, in contrast to morphine, an antispasmodic effect on smooth muscle, including bronchial musculature, and causes very little depression of respiration or of the cough reflex. Despite the enormous amount given, no ill effects were seen, and there were no withdrawal symptoms.

Summary

A case of tetanus treated with C10 and pethidine is presented.

It was found possible with these two drugs to control the spasms, abolish the rigidity, and relieve the pain of tetanus without unduly depressing either respiration or the cough reflex.

The advantages of pethidine as an adjuvant to the relaxant treatment are commented on.

The case is reported in the hope that others may be encouraged to give C10 a further trial. I should be interested to hear of any other cases.

I wish to thank Dr. T. Howard Crozier and Dr. F. Pantridge for allowing me to co-operate in the treatment of this case, and for their help and encouragement; Dr. T. Leitch for his help in carrying out the treatment; and the sisters and nursing staff of ward 15 for their invaluable assistance.

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PROLONGED INTERCOSTAL PARALYSIS DUE TO A RELAXANT

BY

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The following case may be of interest to anaesthetists. As relaxants are only a recent addition to the anaesthetist's armamentarium, any complication following their administration is worthy of record.

Case Report

A woman aged 33 was recently admitted to hospital for hysterotomy and sterilization. Seven years ago, following lobar pneumonia, she contracted acute nephritis, which has since become chronic. Three years ago a pregnancy was artificially terminated owing to the onset of incapacitating symptoms related to her nephritis; and for the past two years she has been subject to intermittent attacks of blurred vision.

Six weeks before admission investigations made at another hospital were reported to her doctor as follows: blood urea, 60 mg. per 100 ml.; urea concentration, less than 2 g.% on all readings; urea clearance test, "very low percentage"; renal function "very poor."

On admission the patient looked well. She had oedema of the ankles; albuminuria + +; her blood pressure was 180/110 and haemoglobin 55%. There was no evidence of cardiac failure or respiratory disease. Pre-operatively, 1 pint (570 ml.) of whole blood was given.

Anaesthesia was induced with sodium thiopentone, 0.4 g. The nose was sprayed with cocaine 15%. Hyperventilation was achieved with nitrous oxide, oxygen, and carbon dioxide, and a No. 8 nasal tube was passed blind. "Flaxedil," 100 mg., was then given, anaesthesia being maintained with a mixture of nitrous oxide and oxygen with minimal cyclopropane. After half an hour the abdominal muscles were beginning to tighten; a further dose of flaxedil, 40 mg., was therefore given. After each dose of relaxant the respirations returned in approximately two minutes. The patient being in the Trendelenburg position, assisted respiration was continued throughout.

After 55 minutes the operation was completed. The patient appeared to be maintaining a good colour, though the respirations were only diaphragmatic. She coughed slightly on extubation and was returned to the ward with an oral airway.

About 10 minutes post-operatively she appeared cyanosed. The colour improved immediately on reintubation and administration of oxygen.

About 1½ hours post-operatively, and shortly after extubation, consciousness returned and the patient asked for a drink. Shortly after this she became unconscious and was breathing "very shallowly." Breath sounds were present in all areas. She was slightly cyanosed. Pulse 130 a minute. Her colour improved with oxygen.

2 Hours Post-operatively.—Blood pressure 260/150. Eyes directed upwards (pupils equal and reacting minimally to light). A provisional diagnosis of hypertensive encephalopathy was made. Respirations diaphragmatic; chest wall sucked in on inspiration. Owing to the presence of moist sounds in the trachea and main bronchi, blind intubation and tracheo-bronchial suction were carried out. Oxygen was given. Magnesium sulphate was introduced rectally and hypertonic sucrose intravenously.

3¼ Hours Post-operatively.—Consciousness returned. Blood pressure 180/110. Patient a little distressed by tube.

3¾ Hours Post-operatively.—Extubated, as good colour was being maintained. Respirations still only diaphragmatic.

5 Hours Post-operatively.—Slightly cyanosed. No improvement in respiratory excursions. Chest wall still indrawn on inspiration. Accessory muscles still active. Conscious. No. 6 tube passed blind after cocainization of nose and pharynx. Tracheo-bronchial tree again sucked out. Patient indicated immediate subjective improvement. From this point onwards the nasal tube was left *in situ* and intermittent tracheo-bronchial suction performed, mucoid material always reaccumulating. The patient's condition appeared to be gradually deteriorating.

9½ Hours Post-operatively.—Blood pressure 220/150. Patient very distressed. Otherwise no change.

10¼ Hours Post-operatively.—E.C.G. showed sinus tachycardia only. Lumbar puncture revealed normal pressure.

12¼ Hours Post-operatively.—Bronchoscopy performed: small amount of mucoid material removed.

13 Hours Post-operatively.—Atropine, 1/100 gr. (0.43 mg.) and neostigmine, 1.25 mg., given. Immediate improvement. Intercostal muscles came into action. Patient quickly returned to "normal." No further post-operative complications.

Comment

Whilst one would not presume to dogmatize about the reason for this occurrence, the following points of interest emerge: (1) Even excessive doses of flaxedil are known (in animals) to be excreted unchanged in the urine—30–100% in two hours (Mushin *et al.*, 1949). (2) The dosage of relaxant, though generous, was not excessive. (3) This patient has very poor renal function. (4) It would appear that the return of diaphragmatic respirations after the administration of flaxedil is not necessarily followed soon by the return of intercostal muscular tone. (5) Further confirmation is given of the fact that inadequate respiratory excursions are not detrimental to the patient provided adequate oxygenation is maintained.

The giving of neostigmine was delayed for two reasons: (*a*) The uncertainty whether it was indicated. Initially, the recovery of consciousness followed by a period of coma with concomitant increase in hypertension confused the picture from the anaesthetic aspect. (*b*) Following this, one was hesitant to administer neostigmine in view of its possible effects on the cardiovascular system.

We await the results of further renal-function tests.

Summary

A case is reported of prolonged loss of respiratory muscular tone following intravenous injection of 140 mg. of flaxedil in a woman with severe renal damage.

The picture is complicated by symptoms suggestive of hypertensive encephalopathy.

I wish to thank Mr. A. Briant Evans and Dr. J. B. Wyman for permission to publish this case.

REFERENCE

Mushin, W. W., *et al.* (1949). *Lancet*, **1**, 726.

In consultation with the Invalid Children's Aid Association, the British Rheumatic Association is now determining how much it should be responsible for the care of children with rheumatic hearts. Local authorities in most areas operate a scheme providing for the medical and educational needs of these children, and, while most can return to their own homes after treatment and convalescence, there remain a small and at present unknown number of children who have either unsuitable homes or none at all. These sufferers, together with mothers of several young children, one of whom may need continuous care, need domestic help to prevent the suffering of either the invalid or the rest of the family. This problem is being taken up by the British Rheumatic Association's local branches. A threefold line of sociological inquiry is now being conducted: one forms part of the research by the Medical Research Council at the London Hospital; another will be based on information provided by the Registrar-General.

Medical Memoranda

Hypertrophy of the Little Finger

In these days, when "compensationitis" is so prevalent and when the examination of patients for insurance claims tends to give the surgeon a somewhat disillusioned opinion about the recovery powers of the average person following trauma, it is refreshing to meet a case such as is described here.

Case Report

A man aged 54 came to the Leith Hospital surgical out-patient department on June 17, 1949. He had fallen off his cycle and bruised his right hand. A radiograph showed a small crack in the metacarpal surface of the right trapezium bone. The injury was of a minor nature, and he made a good recovery with no special treatment beyond supporting strapping for a fortnight.

Radiograph of the patient's hands. Note the thickness of the fifth right metacarpal and the increase in size of the fifth right finger compared with the left.

Attention was drawn, however, to the deformed condition of the right hand, from which the fingers and thumb were absent with the exception of the fifth finger. The patient said that this was the result of a shrapnel wound in France in September, 1918. He had been treated in a field hospital, had had one operation, and had been discharged within a month. When the wound had healed he started work as a miner, and had been employed in the pits for over three years. The scar had not been painful, and he had been able to grip the handle of a shovel firmly between his little finger and the remaining portion of his right hand. After leaving the mines he had continued at various forms of labouring, and had been able to work without difficulty; his present job is lifting bales of paper, etc., in a stationery office. Examination of the right hand showed the little finger to be almost as long as, and actually thicker than, the middle finger of the left hand; it was much larger in every dimension than the left little finger. The patient demonstrated the surprising strength of the grip of his right hand, in spite of the tenderness due to the recent injury. This power was largely owing to the great development of the "opposition" element in the movements of the fifth finger. The fifth metacarpal segment had become hypermobile, with excessive development of the muscles of the hypothenar eminence, so that the fifth finger could be swung across the palm to the first metacarpal, which was relatively fixed.

The scars of the traumatic amputation had healed cleanly without becoming adherent to the stumps of the third and fourth metacarpals, and there had been no development of stump neuromata. The patient had therefore been able to use the hand vigorously from the start without pain. Shorn of all its members save the weakest, the hand nevertheless had been used unsparingly in the one way it could—namely, gripping—and it had responded. The bones of the fifth finger could not grow in length, as the epiphyses were already ossified, but they became thicker and stronger, especially the metacarpal, to which the opponens muscle is attached. The right hand, though only a remnant, is to-day the hand of a strong labouring man. The accompanying radiograph demonstrates the features noted above, particularly the hypertrophy of the soft tissues of the fifth right finger.

This case illustrates the truth of the old adage, "Where there's a will there's a way." It shows how well Nature responds to the demands of a determined man in overcoming gross mutilations. It makes one more than ever sceptical of those patients who come for examination on compensation claims, months after some comparatively minor injury, holding their fingers stiff and useless and their healed scars still swathed in bandages.

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Status Epilepticus: A Symptom Complex of African Trypanosomiasis

The following case, in which the cerebral stage with meningo-encephalitis was complicated by an attack of status epilepticus, is of interest. Few patients present themselves for treatment during the incubation or febrile stage.

Case Report

The patient, a married man aged 33 with two children, was a native of Georgetown, which is in the tryanosomiasis endemic area (138 cases in the first eight months of 1949). He had been a ferryman at the southern crossing of the river at Sankuli Kunda for ten years. He had been in fairly good health, with only irregular attacks of some of the more common diseases—malaria, yaws, etc. The present illness started on June 1, 1949. He had attended the funeral of a friend, and on his return home he suddenly became confused, exhibiting abnormal behaviour and a tendency to sleepiness. Later he grimaced, became apathetic, more confused, rambling in his speech, and difficult to manage at home. He also complained of headache and fever. After an unstable recovery on native methods of treatment, he was admitted to Bansang Hospital on June 20.

On admission he was in a state of acute maniacal excitement. His temperature was 99° F. (37.2° C.), pulse 80, and respirations 20. A general physical examination revealed nothing grossly abnormal in the vital systems. Laboratory investigations showed that malaria parasites were not present in the blood, and that trypanosomes were present in the cerebrospinal fluid and gland juice. His excitement was controlled by 1 g. of hexobarbitone, and a course of "antrypol" and tryparsamide injections was started.

Six days later his condition had greatly improved. After the first injection of 1 g. of antrypol he became sensible, co-operative, well orientated in place, took his food, became interested in his condition, and expressed his gratitude for the care that was taken in his case. This improvement continued for another nine days, until July 5. On the morning of this date he had his third injection (2 g. of tryparsamide). At about 1 a.m. next day he had an epileptic fit which continued for two hours with only a few seconds between the attacks. This status epilepticus was controlled by 1 g. of hexobarbitone intramuscularly. He became somnolent and continued in this state for 36 hours. On recovery he was garrulous, incoherent in his speech, restless, untidy in his habits, refused his food, and was a danger to himself. Another physical examination disclosed no abnormality. The plantar response was flexor.

The excitement continued until July 15. During that time he was agitated, aggressive, noisy, restless, difficult with his food, and cantankerous. He slept for long hours between attacks, which lasted on the average about 20 minutes. On July 18 laboratory investigation revealed that trypanosomes were present in the gland juice and cerebrospinal fluid.

He entered into an apparently lucid period on July 16 and continued fairly well behaved and co-operative till August 8, when he again became noisy and confused and exhibited grotesque behaviour. He was auditorily and visually hallucinated. He spoke to imaginary people around him and complained that they said they were going to kill him. During the relapse on August 8 he had another attack of status epilepticus, and this recurred the following day. The cerebrospinal fluid was again examined, but this time trypanosomes were not present. This relapse lasted only two days, after which he became normal with only an occasional outburst of shouting and delusional displays.

He maintained his improvement and on August 16 inquired whether the man in his place had been informed that he was "well" and would soon go home. He became preoccupied with his discharge from hospital and continually inquired when he would be allowed out. This unstable recovery he maintained until his discharge on September 16. He was facile, childish, mentally retarded, stereotyped in behaviour, but easy to manage. He was discharged to the care of his relatives.

Comment

Trypanosomiasis with epilepsy has already been reported. This case had an additional symptom complex—namely, that of status epilepticus. It is to be noted that these epileptic episodes had no relation to the presence or absence of trypanosomes in the cerebrospinal fluid. It is possible that the attacks were due to a structural damage to the brain itself.

Medical practice in the Tropics is prejudiced by the delay before hospital facilities are sought. This is sometimes due to ignorance and sometimes to fear. It is possible that cases of this nature may not be brought to hospital until an attack of status has begun, or during the post-epileptic somnolent stage, which in the above case lasted for thirty-six hours. In trypanosomiasis endemic areas all patients brought to hospital in epileptic fits or seemingly unconscious must be suspected of having trypanosomiasis in addition to the other more common causes—cerebrospinal meningitis, cerebral malaria, and hysteria.

I wish to thank the Acting Director of Medical Services, Dr. T. P. Eddy, for permission to publish this case, and Dresser-dispenser Wilson for his invaluable assistance in the compilation of the record and for translating the patient's Mandinka.

Edward F. B. Forster, M.D.,
Medical Officer in Charge, Bansang Hospital.

Case of Double-headed Monster

This is a case of twins united by the trunk (thoracopagus and dicephalus).

Case Report

A 3-para aged 25 was at full term. Her first delivery was a breech, the second a vertex, both children being alive and normal. At the antenatal examination the presentation was diagnosed as breech. An unsuccessful attempt at external version was made at 34 weeks, but no further efforts were made as the patient was a multipara and had had a previous successful breech delivery.

Labour started at 4.30 a.m. and she was admitted at 5.30 a.m., when the cervix was near full dilatation. The membranes were intact and both feet could be felt. Labour was allowed to proceed normally. The membranes ruptured at 6.40 a.m. and the first foot was delivered in five minutes, followed by the second with the next pain. The descent of the foetus was slow, but nothing was suspected until a third foot presented at the vulva. On examination another foot was felt and a second pelvis. The patient was fully anaesthetized and a hand was inserted to push up the posterior foetus in order to deliver the anterior twin. This was found to be impossible, and the correct diagnosis was made only after thorough palpation with the whole hand inserted.

As the two pelves were causing obstruction, one was amputated at the level of the superior crest of the ilium. Traction even then failed to effect any progress owing to the size of the trunk, and the second pelvis was also amputated at the same level. This allowed for the compression of the body, and all the four hands were brought down one after the other. The next problem was the delivery of the two heads. I decided to cut off one of them with a hook, and in order to reach it asked my assistant to exert steady traction on the trunk upwards towards the mother's abdomen while I inserted my hand from behind to reach the posterior neck to insert the hook round it.

This manœuvre resulted in an unexpected delivery of both heads one after the other. The convexity of the anterior head fitted in the concavity of the posterior neck, and the posterior head was first delivered over the perineum followed rapidly by the anterior head, thus making the amputation of one of the heads unnecessary.

The third stage was quite normal: the placenta was delivered complete after 10 minutes at 8.10 a.m. There was only one umbilical cord. The perineum was not torn, though there was a good deal of bruising. Penicillin and sulphonamides were given as a prophylactic measure, and the patient made an uneventful recovery.

The Foetus.—Permission to preserve the specimen and for further post-mortem examination was refused. The combined trunk was very big, and the line of fusion of the two trunks is oblique and can be seen clearly in the accompanying photograph. The umbilical cord was inserted between the two pelves. The left anterior hand and the right posterior hand belonged to one of the twins and vice versa owing to the oblique plane in which the two trunks had joined. Both foetuses were female and completely separate from the neck upwards and from the pelvis downwards. The parts were fairly well developed, the total weight being 11 lb. (5 kg.). The heads were also of normal size, and I was surprised at their normal delivery, though the mother's pelvis was roomy.

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Chief Medical Officer, Pandya Memorial Clinic, Mombasa.

Reviews

WEIR MITCHELL

S. Weir Mitchell: Novelist and Physician. By Ernest Earnest. (Pp. 279. £1 8s.) London: Geoffrey Cumberlege. 1950.

We have waited a long time for an adequate biography of Silas Weir Mitchell, America's foremost and first neurologist. Born in Philadelphia in 1829, four years after Charcot, six years before Hughlings Jackson, and sixteen years before Gowers, Weir Mitchell was blessed with robust health and vitality despite the handicap of an essential tremor of his upper limbs. His vigour thus enabled him to endure a long life and a full one, glorying in his achievements as a pioneer in medicine, a novelist, a poet, and a *bon viveur*. Perusal of his life story teaches us that, albeit difficult, it is possible for a neurologist to be a man of culture and sensitivity; that he can live to the advanced age of 84 continuing in a busy consulting practice, and, what is more, continue to be a valuable hospital physician.

The biographer is not himself a medical man, and perhaps the purely technical aspects of Weir Mitchell's career are subordinated so as not to dismay a general reader. We are left in ignorance of many things we should like to know. The first year of postgraduate study was in Paris, but we are not told where. His work abroad must have been a powerful stimulus, for Weir Mitchell was one of the early few who introduced into American medicine the European conception of research. A most competent physician with an overpowering presence, he made a considerable impression, especially upon his large circle of adoring female patients. He was not a good teacher; for his faulty memory compelled him to relearn his material, and he consequently disliked lecturing. His mind was original, suggestive, fertile—"yeasty," as his friend L. Keen put it. He was unlucky in his successive application for professorships in Philadelphia, but no doubt mankind benefited therefrom, for, as Oliver Wendell Holmes said of him, "Perhaps it is hardly desirable that an active man of science should obtain a chair too early, for I have noticed . . . that the wood of which academic fauteuils are made has a narcotic quality which occasionally renders its occupant somnolent, lethargic, or even comatose!"

Although Weir Mitchell was a close friend of Osler, he seems to have been no great admirer of England. Perhaps it is the biographer who is responsible for the acidulated remarks on British weather, which we cannot help, on British cooking, which is fair enough, on the British attitude towards the American Civil War, which is understandable, and on the huge feet of British women, which is absurd.

Weir Mitchell's hospital clinic for nervous disorders was founded in 1861, and hence was the oldest in the States and one of the oldest in the world. His career as a novelist did not begin until he was 51, and he wrote until the time of his death at the brink of 85. His fiction was always of a psychological genre, and he has been compared to Henry James and to O. W Holmes. Though his novels are often problem-studies in human affairs, they are marked by a certain primness—an attitude which the biographer sums up by emphasizing that he was a Philadelphian. His verse, we are told, was undistinguished. Weir Mitchell is associated with the successful treatment of certain neurotic states, a success which is probably due as much to his domineering personality as to his methods. Freud shocked him. After reading a library book on psycho-analytic beliefs Mitchell threw it in the fire, with the protest, "Where did this filthy thing come from?" Weir Mitchell was always a clubman, a socialite, and an assiduous attendant at boards of management. The last-named chore became more and more irksome to him, and eventually he expostulated to his wife that she should engrave upon his tombstone: "Committee'd to Death." This is a warning which modern physicians and surgeons might well take to heart.

MACDONALD CRITCHLEY.

THE BREAST

The Breast. Structure: Function: Disease. Edited by F. D. Saner, M.B., Ch.B.(Camb.), F.R.C.S. (Pp. 316; 193 illustrations. £2 5s.) Bristol: John Wright and Sons. 1950.

Many books, large and small, have been written on diseases of the breast, but this symposium seems to strike a happy medium between bare sufficiency and such prolixity as is suitable only for the extreme specialist. Here within the compass of some 300 pages we find all the essentials of the subject attractively discussed in a manner which is well balanced despite the multiple authorship. Indeed, it may be described as a very competent book of really useful size.

There is a good section on pathology, illustrated by excellent photomicrographs which do not appear to have lost much detail in reproduction. A particularly interesting chapter is that on the importance of spread of carcinoma along the internal mammary lymphatic chain. The author of it recommends that in early cases without extensive axillary involvement an intercostal biopsy should be performed at an early stage of the operation; if the immediate section report is negative a radical operation is carried out, but if the result is positive a simple mastectomy is done, the treatment of the secondary deposits being by radiotherapy.

The whole question of the relationship of surgery to radiotherapy is fully discussed and the final opinion is thus expressed: "The extent and timing of the respective use of surgery and radiotherapy is dependent on the state of the disease and will be subject to adjustment as experience increases, but the merit of a combination of the two methods is undoubted." There is a very useful appendix giving a summary of the statistical data relating to certain aspects of incidence, diagnosis, and outcome of treatment.

The only small criticism which we have to make is that the coloured illustrations, except the colour photographs, should have been omitted. They fail to give a recognizable impression of the conditions they set out to illustrate and in this way are misleading. No doubt they are good art, but a scientific subject like surgery does not allow of any artistic licence.

NORMAN C. LAKE.

VENEREAL DISEASES

A Textbook of Venereal Diseases. By R. R. Willcox. (Pp. 439; 154 figures. £1 12s. 6d.) London: William Heinemann Medical Books. 1950.

The list of appointments, past and present, held by the author of this book is a guarantee that he knows what he is writing about; few, if any, venereologists can have studied venereal diseases in so many parts of the world. The book is admirably put together and the illustrations are excellent, showing what they are meant to show; the coloured plates are exceptionally clear. It will appeal to

venereologists all over the world and can be strongly recommended both for its sound teaching and for its wise advice.

The author ranges over the whole subject and includes accounts of those diseases of the Tropics and subtropics which closely resemble syphilis. He discusses also a number of para-venereal conditions seen commonly in V.D. clinics. The risks and nursing attention required when pyrexia is produced by T.A.B. given intravenously might with advantage have been set out more fully, for the reaction caused may on occasion be alarming to patient, doctor, and nurse. Unfortunately the literary standard of the book falls short of the technical, and more than a hundred errors, many of a minor nature, were noted; for some of these the proof reader must be held responsible.

T. E. Osmond.

DEFECTIVE CHILDREN

Children with Mental and Physical Handicaps. By J. E. Wallace Wallin, Ph.D. (Pp. 549; illustrated. £2 2s.) London and New York: Staples Press. 1950.

This book is intended to supply professional workers in the fields of special education with a modern reference book descriptive of mental and physical disease in children. The author has been for nearly forty years a specialist in the United States in the education of handicapped children, and if he had written only of matters within his special field he might have produced a first-class book.

The first part of the book is concerned with a description of mentally defective children—their types, classification, degrees of educability, and so on. So far as I can judge, these chapters constitute an admirable review, informed by special knowledge and wide experience.

It is impossible to write favourably of the part of the book on physical handicaps. It is composed without expert knowledge, it is peppered with references from old and modern authors indiscriminately selected and to whose papers the author in his preface ingenuously explains that he has not always had personal access, and he is equally undiscriminating in his selection of relevant subjects. For example, he describes such rare diseases as Wilson's disease, gargoylism, the Hand–Schüller–Christian syndrome, epiloia, Tay–Sachs disease, pituitary dwarfism, pubertas praecox, and so on, and yet he does not mention rheumatic heart disease or congenital cardiac disorders. In writing of mongolism the author devotes three pages to some fourteen described causes of mongolism, nearly all of them entirely speculative. In short, any worker who is concerned with handicapped children and who wants information about physical disease in children is advised to consult a standard textbook of paediatrics, whether English or American, rather than rely on the information provided in this book.

D. V. Hubble.

The Medical Annual, 1950 (John Wright and Sons, Ltd., 25s.), is the 68th of the series, and once again the many contributors, under the experienced editorship of Sir Henry Tidy and Mr. A. Rendle Short, have surveyed recent progress in medical science. The aim of the *Medical Annual* is to help the practitioner, and emphasis is of course on the practical aspects of recent developments; but even so this volume is remarkably comprehensive. Cortisone and the new antibiotic drugs are obvious subjects, but space has also been found for, among other things, a full description of the Pulheems system of medical classification and for a brief discussion of the discovery of oestrogen-like substances in clover and grasses. The usefulness of this volume is enhanced by excellent plates (some in colour), a comprehensive index, and a classified list of new books published in Britain and America.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

The Child and the Magistrate. By J. A. F. Watson. (Pp. 367. 12s. 6d.) Revised edition. London: Jonathan Cape. 1950.

A Dictionary of Dairying. By J. G. Davis, D.Sc., Ph.D., F.R.I.C. (Pp. 856. No price.) London: Leonard Hill. 1950.

Principles of Pathology. By R. A. Willis, D.Sc., M.D., F.R.C.P. (Pp. 667. 50s.) London: Butterworth. 1950.

Essentials of Ophthalmology. By R. I. Pritikin, M.D., F.A.C.S., F.I.C.S. (Pp. 561. 60s.) London: J. B. Lippincott. 1950.

The Heights and Weights of Boys and Girls. By A. Sutcliffe, M.A., B.Sc., and J. W. Canham, M.A. (Pp. 80. 10s. 6d.) London: John Murray. 1950.

World Surgery 1950. By S. A. Zieman, M.A., M.D., F.A.C.S., F.I.C.S. (Pp. 177. 50s.) London: J. B. Lippincott. 1950.

Dawson of Penn. By F. Watson. (Pp. 344. 18s.) London: Chatto and Windus. 1950.

Adler's Place in Psychology. By L. Way. (Pp. 334. 18s.) London: George Allen and Unwin. 1950.

The Art of Scientific Investigation. By W. I. B. Beveridge. (Pp. 171. 10s. 6d.) London: William Heinemann. 1950.

The Velpke Baby Home Trial. War Crimes Trials. Edited by G. Brand, LL.B. Vol. 7. (Pp. 356. 18s.) London: William Hodge. 1950.

The Diary of Sylas Neville, 1767-1788. Edited by B. Cozens-Hardy, D.L., M.A., F.S.A. (Pp. 357. 21s.) London: Geoffrey Cumberlege. 1950.

A History of Biology. By C. Singer. 2nd ed. (Pp. 579. 35s.) London: H. K. Lewis. 1950.

Outwitting Your Years. By C. W. Lieb, M.D. (Pp. 318. 9s. 6d.) Kingswood, Surrey: The Windmill Press. 1950.

Thank God for My Heart Attack. By C. Yale Harrison. (Pp. 156. 7s. 6d.) Kingswood, Surrey: The Windmill Press. 1950.

Healing Hands. By E. M. Anderson. (Pp. 72. 2s. 6d.) London: Church Missionary Society. 1950.

One Nation: A Tory Approach to Social Problems. Edited by I. Macleod and A. Maude. (Pp. 96. 1s.) London: Conservative Political Centre. 1950.

Man and His Environment. By A. L. Banks, M.A., M.D., F.R.C.P., D.P.H. (Pp. 16. 1s. 6d.) London: Cambridge University Press. 1950.

New Biology, 9. Edited by M. L. Johnson and M. Abercrombie. (Pp. 128. 1s. 6d.) Harmondsworth: Penguin Books. 1950.

Blindness: Modern Approaches to the Unseen Environment. Edited by P. A. Zahl. (Pp. 576. 48s.) Princeton, New Jersey: Princeton University Press. 1950.

Medicinal and Food Plants of British Columbia. By I. Bastow Hudson, M.B., B.S., M.R.C.S., L.R.C.P., L.M.C. (Pp. 70. 10s.) Victoria, B.C.: I. Bastow Hudson. 1950.

Factors Regulating Blood Pressure. Edited by B. W. Zweifach and E. Shorr. (Pp. 280. No price.) New York: Josiah Macy, jun., Foundation. 1950.

Child Care in Israel. Edited by C. Frankenstein. (Pp. 324. No price.) Jerusalem: The Henrietta Szold Foundation for Child and Youth Welfare. 1950.

Allergie und Praxis. By G. A. Rost, M.D. (Pp. 191. M. 15.60.) Berlin: Springer. 1950.

Das Magen-Zwölffingerdarmgeschwür und seine Behandlung. By M. Friedemann, M.D. Completed and edited by H. Schloessman. (Pp. 218. M. 16.50.) Jena: Gustav Fischer. 1950.

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ANTICOAGULANT THERAPY OF ACUTE MYOCARDIAL INFARCTION

In assessing the value of any form of treatment for acute myocardial infarction it is essential to be closely familiar with all the details of the natural course of the disease. Failing this, the treated series must be compared with a like series of untreated controls. This platitude will be forgiven by those who realize the great difficulty in obtaining so simple a thing as the natural mortality rate for acute myocardial infarction and the many uncertainties that surround controls. Mortality figures given in the literature are mostly based on hospital experience, and vary from 8% for first attacks treated by means of rest and a low-calorie diet[1] to 78% in young adults.[2] Unless details are known, crude mortality figures mean little. For example, the largest series quoted by Drs. J. A. Tulloch and A. Rae Gilchrist in their article at page 965 is that reported by Yater and his colleagues,[3] in which the crude mortality rate was 50% of 866 cases. These patients were all under 40 years of age and all men. They were collected by the U.S. Army Institute of Pathology and the Veterans Administration. In 450 cases the diagnosis was established by necropsy; of these, 223 died abruptly or within 15 minutes, and another 45 died between 16 minutes and 2 hours. Thus more than half of the fatal cases would have been reported to the coroner in civil life. If all the immediate survivors had been sent to hospital, the mortality rate calculated by the hospital staff could not have exceeded 30%. Then, of the total of 866 patients, only 75 (8.6%) died after the first 24 hours. Again, while most fatal cases must have been included in the series, owing to the manner in which the material was collected "cases of many living patients were excluded because of inadequate data." The details of this large series therefore indicate that in American soldiers under 40 years of age acute myocardial infarction causes instant death in 16%, almost immediate death (within 15 minutes) in an additional 10%, and death within two hours in a further 5%. Of the remaining 598 patients who would have had a chance of reaching hospital and obtaining treatment, 107 or 18% died within 24 hours and 12.5% died afterwards of the acute illness. This gives a very different impression from the 50% mortality figure originally quoted. Similar data are needed about older men and women in civil life.

Anticoagulant therapy for acute myocardial infarction is now widely practised, and since it is an expensive and troublesome form of treatment there should be general agreement about its value. Tulloch and Gilchrist describe the treatment of 70 patients and compare the results obtained with the behaviour of the disease in 84 control subjects. Their claim that anticoagulant drugs reduce the mortality rate of acute myocardial infarction by one-half, and the incidence of thrombo-embolic complications also by one-half, must receive very close attention. Their conclusions are based on careful and well-presented work, and their controls appear to fulfil all requirements. Moreover, the same conclusions may be drawn from data which they have collected from the literature. Yet there may still be some who are not quite satisfied, or who feel that anticoagulants should be reserved for particular cases rather than used routinely. By far the largest treated series in the literature is that collected and reported by a special committee set up by the American Heart Association.[4] This series comprised 432 cases, and results were compared with those obtained in 368 controls. The mortality rate was 24% in the controls and 15% in the treated group. The difference was attributed chiefly to a reduction in thrombo-embolic deaths—3% in the treated patients and 10% in the controls. The incidence of thrombo-embolic manifestations was 25% in the control group and 11% in the treated group. Comparisons between the two series for each week of the disease were equally impressive up to the end of one month. An important finding was that the mortality rate was reduced by anticoagulants only in patients over 60 years of age. But thrombo-embolic complications were greatly reduced in all patients.

These results look impressive, and the controls seem strictly comparable: moreover, it is just the kind of result that would be expected. Yet there are one or two disturbing features. Independent studies do not put the death rate from pulmonary embolism as high as these figures suggest. Eppinger and Kennedy,[5] for instance, found it was 6.5% in 200 fatal cases of acute myocardial infarction, and Hellerstein and Martin[6] 12% in their series of 160 necropsies. If the total mortality rate was around 25%, then pulmonary embolism could have caused death in only 2–3% of all cases encountered.

[1] Master, A. M., *Amer. Heart J.*, 1936, **12**, 549.
[2] Newman, M., *Lancet*, 1946, **2**, 409.
[3] *Amer. Heart J.*, 1948, **36**, 334.
[4] Wright, I. S., *et al.*, ibid., 1948, **36**, 801.
[5] *Amer. J. med. Sci.*, 1938, **195**, 104.
[6] *Amer. Heart J.*, 1947, **33**, 443.
[7] *Amer. J. med. Sci.*, 1948, **216**, 172.

This does not tally with the 10% incidence quoted above. Again, Hellerstein and Martin found clinically detectable thrombo-embolic lesions in 11.5% of 1.605 cases of acute myocardial infarction collected from the literature. This makes an interesting comparison with the incidence of 11% found in Irving Wright's series treated with anticoagulants.

Tulloch and Gilchrist calculated the crude mortality rate in their control patients to be 40%. In the series reported by Wright and his colleagues it was as high as this only in persons over 70 years old, being 30% in those between 60 and 70 and only 10% in those under 60. The mortality rate was nearly 50% in Tulloch and Gilchrist's 53 controls over 60 years old, and 28% in their 32 controls under 60. The difference between the two series is probably explained by the large number of admissions within the first 24 hours in the Edinburgh group (33%). Immediate admission to hospital was almost certainly uncommon in the American series; otherwise the mortality rate in the first week would have been appreciably higher than that in the second, whereas they were practically the same. One of the most impressive features of the Edinburgh series is the close similarity of the treated and untreated groups in duration of the illness prior to admission. The chief difficulty about accepting Tulloch and Gilchrist's conclusions arises from a study of the causes of death in their series. It will be seen that 20% of the controls and 21% of the treated patients died suddenly or from heart failure. This is the expected incidence, and it must be generally agreed that these are the chief causes of death in acute myocardial infarction among those not dying from shock, and that anticoagulants would not prevent the last. The higher mortality among the controls was caused by three deaths from persistent shock or coma, five from a recurrence of myocardial infarction, and six who died in the first 24 hours. Could these have been prevented by anticoagulant therapy? Clearly dicoumarol could not have prevented the six immediate deaths, but heparin might have done. A detailed analysis of the early mortality rate in those treated with heparin and in matched controls is required. Could dicoumarol have prevented "recurrent myocardial infarction"? According to Selzer[7] only 2% or 3% of patients with acute myocardial infarction die from secondary coronary thrombosis.

In the light of present evidence it is by no means certain that anticoagulants should be used as a routine in all cases of acute myocardial infarction, and it would be a pity if no further comparisons with controls were made. That anticoagulant therapy may be of great value can scarcely be doubted, but future work may well show that, like any other drug, it is indicated only in certain well-defined circumstances.

PAY IN THE SALARIED SERVICES

During its struggle to obtain fair remuneration for general practitioners the B.M.A. has not neglected the claims of other branches of the profession. Earlier this year we referred to the unsatisfactory outcome of discussions with the Defence Departments[1] about the pay of medical officers in the armed Forces, but the Minister of Defence has since received a deputation from the B.M.A. and stated that he and the other Service ministers were sympathetic with the Association's case, though they were not convinced that improvement of pay was necessarily the only answer to the problem of recruitment of medical officers.[2] Last week the Government's readiness to face the facts became still more apparent during the debate in the House of Lords on the subject of man-power in the medical services (reported on page 1005). Lord Haden-Guest pointed out the difficulty of efficiently maintaining the health services in the armed Forces and the Colonies when 90% of the doctors in the country were working in the N.H.S. He suggested that every doctor, wherever he was employed, should be eligible for the same rates of pay and the same pensions. Lord Moran, continuing the argument on behalf of the specialists, said that the natural remedy for the scarcity of specialists in the R.A.M.C. was to make conditions such that they would attract specialists in the open market—in other words, to pay them more. Lord Webb-Johnson thought that secondment of doctors in the N.H.S. to the Forces and Colonial Medical Service should be possible, and also secondment in the opposite direction. Lord Shepherd, who replied for the Government, said it was now realized that there must be a movement of wages and salaries, and he was hopeful that among the claims that would be met would be that for medical men in the Services, not merely because the cost of living had increased, but because it was right that they ought not to be worse off than medical men in civilian life. This is an important admission from a Government spokesman, for it implies that the rates of pay in the N.H.S. are to be the yardstick by which rates in other medical services should be calculated.

Members of another salaried service—the public health service—have also for long been dissatisfied with their remuneration, and here again scarcity of recruits has been causing concern. In their claims for better pay medical officers of health and their assistants have had the full support of the profession. Among doctors there should be no argument about the relative importance of prevention and treatment—both are vital for human welfare. When the staff and management sides of Committee C of the Medical Functional Whitley Council failed to agree on revised salary scales the case was

[1] *British Medical Journal*, 1950, 1, 1184.
[2] Ibid., *Supplement*, 1950, 2, 29.

taken to the Industrial Court, which is still sitting. The evidence for the staff side has been collected by the B.M.A., working, of course, in close association with the Society of Medical Officers of Health. Medical men and women in the public health service are not the only ones who will eagerly await the Court's findings. No one wishes to see the various branches of the profession graded in descending stages of public regard.

TECHNIQUE IN B.C.G. VACCINATION

Many have tried to obtain statistical evidence of the efficacy of B.C.G. vaccination, but few have succeeded. The number of factors that influence the susceptibility of the individual to tuberculous infection is large, yet all these variables must be taken into account if the figures are to pass the statistician. Race, age, degree of exposure, intercurrent infections, housing conditions, predisposing occupations, and nutrition are unavoidable extraneous factors in any investigation. If differences of technique of individual vaccinators have also to be considered, statistical analysis of the results becomes impossible. Such differences, however, can be eliminated by standardization. The difficulties faced by those who have the task of evaluating the results of B.C.G. vaccination have been well summed up by Ustvedt,[1] in commenting in a recent issue of the *Bulletin of the World Health Organization* on the work of what is known as the Joint Enterprise. This organization, manned by Scandinavian teams, financed by Unicef, and advised by W.H.O., has been fighting to check the spread of tuberculosis in war-devastated Europe during the past two years. It plans to carry out tuberculin tests on over 30,000,000 children and young adults and to vaccinate all negative reactors. In spite of great difficulties the work of the organization has made rapid progress, but it is not surprising that records generally, and details of technique in particular, should be incomplete. Ustvedt writes:

> Of course, no conclusive answer to any of these complicated questions can be given from the experience so far gathered within the Joint Enterprise. On the whole, I would rather say that the very fragmentary information which has been collected up to now, and which is mostly of limited value, has pointed to a series of problems, and has given some evidence in certain directions, so that a more systematic exploration of this subject can be planned and carried out.

In the next phase of the campaign the W.H.O. Tuberculosis Research Office in Copenhagen is planning an investigation of these problems, under controlled conditions.

In the same issue of the *Bulletin* Van Deinse and Sénéchal[2] draw attention to another variable factor in B.C.G. vaccination. The vaccine, when maintained on Sauton-potato as advised by the Institut Pasteur in Paris, has an average length on the tenth day of subculture of 3 μ. At the State Serum Institute in Copenhagen, where the vaccine for the Joint Enterprise and for this country is prepared, the stock culture is maintained throughout on Sauton's liquid medium, and some difficulty has been found in regulating its speed of growth and maintaining the constancy of its allergizing properties. Van Deinse and Sénéchal found that the average length of the Danish bacillus on the tenth day is only 2 μ. It would appear from this that if the decrease is only in the length of the bacillus the Danish vaccine contains one and a half times as many bacilli as the same weight of the French; if the decrease occurs uniformly in its other two dimensions as well there would be over three times as many organisms in an equal weight of the Danish vaccine. In any standardization of technique this fact must be borne in mind.

About a year ago we pointed out[3] the urgent need for controlled B.C.G. trials, for the introduction of B.C.G. vaccination into this country gives a new opportunity to collect evidence which will stand statistical scrutiny. The Ministry of Health has decided to issue B.C.G. in the first instance only to selected vaccinators for use on contacts, nurses, and medical students, and detailed records are to be kept. Much of the technique has been standardized, for the vaccine is obtained from only one source and is suitable only for intracutaneous vaccination. But, though the Ministry's memorandum[4] lays down the criterion for a positive reaction in each test, it leaves the individual vaccinator free to decide whether he will vaccinate those in whom negative results are obtained to any of the following tests: the jelly patch test, the adrenaline-Pirquet, the Mantoux 10 TU (1 TU=0.01 mg. O.T.), or the Mantoux 100 TU (using P.P.D. or standard Old Tuberculin). In at least one hospital region (Oxford) a scheme has been evolved to follow the Ministry's recommendations, but with a stricter standard of technique. It has been mutually agreed throughout this region that a person shall not be classified as a negative reactor, whatever his age, until he has failed to show a positive reaction to a Mantoux test with 1 in 100 standard Old Tuberculin, read after 72 hours. The dosage and time intervals for conversion tests and the revaccination of those who remain tuberculin-negative have also been standardized. Though the enforcement of a rigid regime would be contrary to the traditional freedom of the medical profession in this country, a detailed model scheme would be welcomed by vaccinators new to B.C.G., and would help them in the planning of their work. Moreover, unless we learn from the mistakes of others and exclude all unnecessary variables, we too, in this country, may fail to demonstrate convincing statistical results.

[1] *Bull. World Hlth Org.*, 1950, 2, 355, 441, and 469.
[2] Ibid., 1950, 2, 347
[3] *British Medical Journal*, 1949, 2, 1278.
[4] Ministry of Health Memorandum 322/B.C.G. (revised).

TREATMENT OF TETANUS

The necessity for giving tetanus antitoxin and penicillin in the treatment of tetanus is fully established, but the best method of controlling the severe and generalized muscle spasms is still debatable. The two possibilities are the use of sedatives and hypnotics, which have a general depressant action on the central nervous system, or the use of substances which have the power of causing muscular relaxation without a general sedative effect. The sedative which is chosen must act rapidly, must not be cumulative, and must not cause undesirable side-effects when given over a period of days or even weeks. For a time "avertin"[1] was the most-favoured sedative, but thiopentone now seems more suitable, and repeated intravenous injections, supplemented if necessary by intramuscular paraldehyde, will control the muscular spasms in many cases. Harris and her colleagues[2] continued with this form of sedation for 15 days in a patient who finally recovered. These authors advocate tracheotomy at the first stage of respiratory embarrassment—an operation which was first suggested by Curling[3] in 1836 and first used by Humphrey[4] in 1856. Laryngospasm and accumulation of viscid bronchial secretions are a real danger in tetanus, and there may be difficulty in keeping the airway free. Suction of the bronchial secretions can be carried out through a soft rubber catheter passed through the tracheotomy tube, and in this way repeated intubation of the larynx can be avoided.

If it were possible to control the muscular spasms by the use of a drug with a specific action without causing cortical depression there would be obvious advantages, since prolonged sedation enhances the danger of the pulmonary complications, which are referred to above. Curare is said to have been first used in this disease by Spencer Wells[5] in 1859, but little further interest in its use was taken till the work of West[6] and Cole[7] in the nineteen-thirties. The preparations of curare at that time were not reliable, and in 1936 Cole felt that prolonged sedation with avertin was safer than the use of curare. Since then more reliable curare preparations have become available, and a number of cases of tetanus have been reported in which its use has been of real value in controlling the muscle spasm. Curare is best given intramuscularly in the form of D-tubocurarine chloride in wax and peanut oil, for in this form it is slowly absorbed and acts for 18 to 24 hours.[8] The most obvious action of curare is its peripheral blocking action at the myoneural junction, but it may also have a local histamine-like action at the site of injection. When given over a long period curare is said to have caused symptoms resembling those of shock in some patients.

The action of tetanus toxin is a central one on the synapses of the spinal cord,[9] while the action of curare is peripheral. This suggested that "myanesin" (α-β-dihydroxy-γ-(2-methylphenoxy)-propane), which is thought to have a central depressant action on the cord synapses, might be preferable to curare, and it was first used in two cases of tetanus by Belfrage.[10] Further reports[11 12] have confirmed its value, but there is some doubt about the most suitable method of administration. Myanesin acts best when given intravenously, but there is some danger of venous thrombosis—though this can usually be avoided with adequate dilution—and of the production of haemoglobinuria, which is usually transient. Myanesin will act when given by mouth in large enough doses, and in this issue of the *Journal* Drs. M. L. Newhouse, J. D. Rochford, and G. Riddell Royston describe two cases of tetanus in which the oral method was used with satisfactory muscle relaxation. They are careful to point out the danger of oral administration if the myanesin is not adequately diluted. The drug has a local analgesic effect in addition to its central action, and in one of their patients pharyngeal analgesia resulted, with an aspiration pneumonia as a consequence. Also in this issue Dr. R. McD. S. Keir describes the use of yet another muscle relaxant in the treatment of tetanus—decamethonium iodide, or C10. This drug appears to depress respiration less than does curare, and also has less of a histamine-like action. In this one patient C10 together with pethidine controlled the spasms, abolished the rigidity, and relieved the pain without unduly depressing respiration or the cough reflex, and it certainly merits further trials in tetanus. There is no doubt that combined treatment with one of these muscle relaxants together with a sedative is the most suitable method of controlling the muscle spasms, for in this way much smaller doses of sedative are effective than if no muscle relaxant is used.

1 Cole, L., *British Medical Journal*, 1942, **2**, 550.
2 *Pediatrics*, 1948, **2**, 175
3 *Treatise on Tetanus*. London. 1836.
4 *Ass. med. J. London*, 1856, **4**, 158.
5 Beaven, D. W., and Dobson, D. J., *N.Z. med. J.*, 1950, **49**, 24.
6 *Lancet*, 1936, **1**, 12.
7 *British Medical Journal*, 1936, **1**, 1191.
8 Weed, M. R., Purvis, D. F., and Warnke, R. D., *J. Amer. med. Ass.*, 1948, **138**, 1087.
9 Sherrington, C. S., *Integrative Action of the Nervous System*. New York, 1906.
10 *Lancet*, 1947, **2**, 889.
11 Torrens, J. A., Edwards, P. M., and Wood, M. W. W., *Lancet*, 1948, **2**, 807.
12 Davison, M. H. A., Ward, A. B., and Pask, E. A., *British Medical Journal*, 1949, **1**, 616.

SMOKING AND PEPTIC ULCER

While it has never been proved, many believe that excessive smoking is a cause of peptic ulcer. The late Sir Arthur Hurst[1] pointed out that "a large majority of patients with duodenal ulcer have smoked excessively for years." There is, however, more general agreement that smoking delays the healing of ulcers, and some physicians forbid smoking during treatment. Support for this comes from the work of Batterman and Ehrenfeld,[2] who have studied the effect of antacid therapy in 108 patients, comparing its success in non-smokers and smokers. They divided the results of antacid therapy into four groups, ranging from those whose symptoms were completely alleviated and who had no acute exacerbations, to those who obtained no relief and who had frequent exacerbations. Among 43 smokers there was an excellent response to antacids in only 47%, while among 52 who were either non-smokers or who did not smoke during treatment an excellent response was observed in 85%. There were 13 patients who resumed smoking when clinical improvement occurred, and of these 11 immediately became worse when they began to smoke again. Further evidence was obtained by giving 28 patients who were smokers cigarettes containing tobacco from which much of the nicotine was removed. These patients had been studied for long periods previously, and only six of them were improved by antacid therapy when they continued to smoke ordinary cigarettes. But when they

1 *Gastric and Duodenal Ulcer*, 1929. London.
2 *Gastroenterology*, 1949, **12**, 575.
3 *J. Lab. clin. Med.*, 1941, **26**, 1322.
4 *J. Pharmacol.*, 1949, **95**, 145.
5 *Brit. J. Pharmacol.*, 1949, **4**, 313.
6 *British Medical Journal*, 1945, **1**, 403.

changed to the processed cigarettes 22 of the 28 immediately improved, and in 11 all symptoms were arrested. A final experiment was made in which 18 of the 22 patients who had improved were given ordinary cigarettes once more, though these were prepared to look like processed cigarettes: eight of these patients then became worse. These results suggest that smoking neutralizes the effect of antacid therapy and that it does so in proportion to the amount of nicotine in the tobacco.

There is much difference of opinion about the amount of nicotine which enters the blood when cigarettes are smoked. Pierce,[3] using a chemical method of estimating the nicotine in the smoke, gives the figures of 2.3 to 3.6 mg. for the amount of nicotine absorbed after deep inhalation of one cigarette, this being about 90% of the nicotine entering the mouth. Even without deep inhalation he estimated that 2.9 mg. is absorbed. Wolff, Hawkins, and Giles[4] measured the nicotine present in the blood of 15 students after they smoked 20 cigarettes in seven hours: they found an amount equal to 0.14 mg. per litre. If the conclusions of Pierce were correct each subject would have absorbed about 60 mg., and this, if distributed through all the body water, would have amounted to 1.0–1.5 mg. per litre. Wolff and his colleagues conclude that there is a rapid destruction of nicotine during smoking. If, however, the destruction is not rapid, the finding of 0.14 mg. per litre indicates that 20 cigarettes have provided 8–12 mg. of nicotine; this agrees well with figures obtained by Ling and Wynn Parry,[5] who found that the amount of nicotine entering the mouth from one cigarette is about 1 mg. Their estimates were made by tests on the blood pressure of the spinal cat and were specific for nicotine. In two investigations undertaken at an interval of 13 years very similar results were obtained. Some experiments by Burn, Truelove, and Burn[6] give guidance about the proportion of nicotine actually absorbed. They observed that the antidiuretic effect of one cigarette in a man, smoked at the height of a water diuresis, was about the same as that of the intravenous injection of 0.5 mg. of nicotine given on another occasion to the same subject. These results suggest that 1 mg. of nicotine enters the mouth from one cigarette and that about half is absorbed when the smoke is inhaled.

MULTIPLE PRIMARY NEOPLASMS

Several examples of multiple carcinoma have been reported in recent correspondence in the *Journal*.[1] The subject has attracted attention for many years as much because of its supposed bearing on the problems of susceptibility and resistance to cancer as because of its interest to the practising surgeon. Further, several substances are now known which will regularly induce multiple tumours in experimental animals: such are acetylaminofluorene and the aminostilbenes.

Estimates differ on whether multiple malignancy occurs more or less often than expected on the basis of chance coincidence alone. The incidence in large series of cases of malignant disease has been variously assessed as between 0.3% and 7.8%, the wide range reflecting differences in the composition of the material. The higher estimate suggests an inherited or acquired susceptibility to cancer, the lower that a primary tumour may confer resistance against the development of fresh primaries. To increase accuracy many writers have included only post-mortem cases of all combinations of multiple malignancy which have been proved histologically, and have estimated the overall incidence among all patients with cancer coming to necropsy within the period under review. There are two objections to this approach—the first concerned with the collection and interpretation of the figures, the second with the validity of the method.

Any estimate of the chance incidence of multiple malignancy in a given population should be based on accurate morbidity figures for each kind of single cancer included in the survey. Such estimates are still of only approximate accuracy, even for the commoner forms in which morbidity figures closely approach mortality figures. Post-mortem series, in spite of increased diagnostic reliability, are of limited value because they are selected fractions of hospital populations, rarely representative in a statistical sense of the geographical populations from which the patients come.

The varied composition of series of multiple malignancies also introduces a source of confusion. Thus some include multiple lesions arising in the same tissue, such as skin, stomach, or large bowel; others exclude these as differing in kind from multiple lesions arising in distinct tissues such as tongue and prostate.[2] Multiple malignancy arising in paired organs such as breasts, gonads, and kidneys is accepted by some, rejected by others. In Slaughter's series[3] of 1,868 cases of multiple malignancy, 54.4% occurred in the same or paired organs, whereas Burke[4] excluded these, as well as Hodgkin's disease, lymphosarcoma, and leukaemias. In all series tumours of low or doubtful malignancy are omitted, yet in a biological problem involving questions of predisposition or resistance the utilitarian clinical concept of "benign" or "malignant" growth is artificial, and common "benign" tumours, though practically of little consequence, might be highly relevant for a full understanding of cancer pathogenesis. But they are unrecorded, and their true incidence is unknown.

Apart from such errors, it is doubtful whether knowledge of the bulk frequency of multiple neoplasms would be of value. Tumours vary greatly in their habits of growth and spread, and in their age, sex, social, geographical, and occupational incidence, and there seems little justification for thinking in terms of susceptibility or resistance to neoplasia in general. The strong hereditary influence present in retinoblastoma, and apparently in a few families with a high incidence of mammary carcinoma and of alimentary neoplasms[5] other than those associated with polyposis coli, is notably absent in the majority of neoplasms. Occupational factors are more prominent in some neoplasms than in others, and the same may be said of hormonal factors. Perhaps some forms of primary tumours will be found to coexist more often than would be expected by chance alone, and other combinations may occur less frequently. In other words, to be biologically valid the statistical analysis of multiple primary neoplasms must be carried out separately for every combination of types, the morbidity of each of which will need to be more accurately known than at present.

[1] *British Medical Journal*, 1950, 1, 648, 905, 1318, 1430; 2, 107, 297
[2] *Lancet*, 1950, 1, 405.
[3] *Surg. Gynec. Obstet.*, 1944, 78, 89.
[4] *Amer. J. Cancer*, 1936, 27, 316.
[5] Ibid., 1936, 27, 434.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

MIGRAINE

BY

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What is migraine? Neurologists are apt to differ in their ideas upon this point. Some physicians would restrict this term to recurring unilateral headaches preceded by visual phenomena and associated with vomiting. Nowadays most would incline to a more catholic conception. More accurately one might define migraine as "a habit of recurring headaches, often one-sided, but not necessarily so; constitutional in nature, inherited, and bearing a vague association with personal or family 'allergic' tendencies and a still vaguer one with epilepsy." Taking an even broader viewpoint, however, we recall that in later life a migrainous sufferer may lose his headache; but recurring visual phenomena may betray the continuance of attacks, or attacks of headache may be replaced by bouts of Ménière-like vertigo. Thus it is that migraine without headache may occur.

Some neurologists isolate a type which might be called "symptomatic migraine." Here the patient develops migrainous attacks in middle life, associated with some morbid anatomical peculiarity, often of a vascular nature. In this connexion a cerebral aneurysm is important, but still more so a cortical angioma. For this reason some cases of migraine should be suspect, and demand special methods of study, if their true nature is to be revealed and the appropriate treatment instituted.

"Symptomatic Migraine"

What are the features which suggest a "symptomatic" as opposed to an idiopathic or constitutional migraine? In the first place, migraine-like headaches starting in the middle-aged or the elderly are not usual, and special scrutiny is advisable. Secondly, headache which is always strictly localized to one area of the skull (and does not change from one side to the other, as is so often the case in simple migraine) should be suspect. Thirdly, migrainous headaches associated with a pulsatile type of tinnitus suggest an angioma. Fourthly, migraine coupled with cranial nerve palsies, whether transient or persistent, should make one think of an aneurysm.

In all such cases there should be a particularly thorough examination of the nervous system, preferably repeated. The fundus oculi may show no abnormality at the first interview, but the wise physician will repeat his ophthalmoscopic examination from time to time. To the routine neurological testing should always be added a careful auscultation of the skull in an effort to pick up a cranial bruit. Still seeking to exclude or confirm the diagnosis of a vascular anomaly of the brain, one has recourse to various technical aids. Electro-encephalography may help by revealing a focus of abnormal cortical activity. Air-studies will occasionally prove informative. Most promising, however, is the result of percutaneous cerebral arteriography. These last two investigations will necessitate the patient entering a special neurological clinic for a few days.

The Migrainous Constitution

The belief is widespread that migraine represents an inborn type of reaction to a number of stresses, both psychological and physical. Just as some rare persons seem to be immune from headache and may survive a long life without experiencing this particular affliction, so there are others—considerably many more—who belong to the category of "headachy subjects" like others in their family. Such persons are apt to develop their headache on every slight occasion; but in addition they may also experience a headache periodically, as it were, and without demonstrable cause. It is probable that the majority of these "headachy" subjects are victims of migraine in more or less outspoken fashion.

There have been various attempts to identify a migrainous habitus and a migrainous personality. None of these can be said to be altogether satisfying, and some of the descriptions indeed are mutually contradictory. Some would correlate migraine with a psychosomatic affection. There can be no doubt whatever that psychological factors may be effective in precipitating an attack of migraine in a migrainous subject. It is possible, too, that migrainous persons have certain identifiable psychological traits which distinguish them from the common herd. But neither of these arguments, singly or together, can justify the doctrine of migraine as a straightforward psychogenic affection, curable by psychotherapy.

Migraine as a Minor Malady

Some patients are fortunate, so far as their migraine is concerned, in that their symptoms scarcely warrant medical attention. Here belong those patients whose headache is mild in intensity and is not incapacitating. If the patient is able to continue his work with little if any falling off in efficiency, then the headache must be rated as mild. Where the headache is relieved by small doses of mild analgesics (e.g., aspirin 10 gr.—0.65 g.) the migraine must be regarded as trivial. When the attack is unaccompanied by vomiting the degree of incapacity is reduced, and unless the headache is intense the migraine may perhaps be regarded as minor in character. Very infrequent attacks—attacks which are promptly relieved by some simple common-sense measure such as the correction of refractive error—also belong within the cadre of minor migraine. Finally one may mention those cases in which the attack is represented by nothing more than short-lived attacks of teichopsia (without headache, dizziness, nausea, or vomiting).

Unfortunately, these foregoing cases would seem to be in a minority, unless it is that they exist without coming to the notice of the family doctor.

Migraine as a Major Malady

The other extreme may be considered—namely, where the migraine threatens the mental or physical health of the victim, upsets the tranquillity of the household, and interferes with working efficiency. Such cases may be spoken of as "migraine major," and they include:

(*a*) Cases where each attack causes much incapacity, by reason of intense and long-continued pain, loss of sleep, intractable vomiting, and anorexia.

(*b*) Cases of "status hemicranicus," where one attack follows another over the course of weeks.

(*c*) Cases of "migraine-epilepsy," in which a syncopal attack, or even an epileptiform seizure, arises in the course of the migraine.

(*d*) "Chronic migrainous debility," where severe attacks recur at frequent intervals and lead to a state of ill-health. The syndrome, which comprises loss of weight, poor appetite, anaemia, debility, lassitude, and depression, is perhaps most often seen in middle-aged women. It is a form of ill-health which may have far-reaching personal, domestic, and social repercussions, and the medical attendant often despairs of affording relief.

There is possibly some relationship between long-standing and severe migraine and a late development of cerebral arterial changes. This doctrine has been put forward, but so far no statistical evidence can be adduced either in support or in refutation.

When a middle-aged sufferer from migraine begins to show an increase in the severity or frequency of the attacks, or if the headache alters in quality and becomes more persistent even though perhaps milder, it is well to suspect an incipient hypertension complicating the picture.

Treatment

In the article on "Headache" contributed to this series by Dr. J. Purdon Martin the treatment of migraine was discussed. Only a few remarks are therefore necessary here. As regards the relief of an attack, one can state that in some mild cases acetylsalicylic acid will suffice. In more severe cases one will need recourse to tab. codein. co.—up to 10 tablets a day. High doses of this sort may dull the severe pain and allow the victim to continue at work. The resulting constipation and flatulency will also need palliative treatment.

The most efficacious measure is an intramuscular injection of ergotamine tartrate, given very early in the attack. It has certain drawbacks in that by reason of the natural history of the disease the first symptoms usually wake the patient unduly early—that is, at an hour when the medical attendant should still be in his bed. If the injection is delayed too long it may be relatively ineffectual. In many patients a good deal of malaise results, and vomiting is frequent. The attack of migraine may be curtailed—at least so far as headache is concerned—but the victim may have to lose a morning's work because of the drug-effect. Ergotamine tartrate by mouth, in hourly doses up to six, is often advocated, but rarely, I have found, with any great benefit. In my experience the same disappointing results have followed the oral use of drops of dihydro-ergotamine tartrate.

The patient with an acute attack of migraine will probably wish to rest in bed in a quiet and darkened room, but unfortunately sleep does not necessarily bring relief. Alcohol and smoking should be shunned during an attack, and indeed most sufferers will do their best to avoid a smoking compartment or any atmosphere tainted with tobacco smoke.

Prevention of attacks of migraine by medicinal means is often most disappointing. The total situation (including type of work, psychological stresses, visual strain) is the most potent adverse factor, which, if it cannot be avoided or suitable adjustments cannot be made, can rarely be neutralized by artificial—i.e., pharmacological—means.

Perhaps phenobarbitone is the safest bet. It should be prescribed in the form of 1 gr. (65 mg.) regularly each night on retiring. Little, if any, benefit results from the administration of this drug at the time of an attack. The patient should persevere for two or three months before concluding that the drug is without avail. If "dopiness" is complained of in the morning, the tablet can be given a little earlier.

A large number of other preparations have been advocated for long-term treatment—thyroid, ovarian and pituitary hormones; urea; carbachol; liquor trinitrini; ergotamine tartrate; bile salts; antihistamine preparations; peptone injections; and so on. At times one or other of these seems to be beneficial, but only exceptionally. It is almost axiomatic that if a patient with migraine fails to respond dramatically to common-sense rules of hygiene, the correction of refractive errors, and phenobarbitone at night, then the doctor and the patient are both in for trouble: the case will probably prove most intractable.

Mention should, however, be made of autohaemotherapy, which is worth a trial in severe cases not responding to medicinal treatment. In some instances the benefit therefrom has been dramatic.

We are still not certain whether the so-called "histamine headache" represents a variety of migraine or not. In any case, for periodic headaches of the type described by Eszenyi-Halasy in the *British Medical Journal* of June 25, 1949 (p. 1121), a regime of desensitization with graded intramuscular doses of histamine is worth while. The patient needs to lie up during this time.

PAEDIATRICS IN THE HARVEIAN AGE

SIR LEONARD PARSONS'S HARVEIAN ORATION

Sir Leonard Parsons, F.R.S., delivered the Harveian Oration at the Royal College of Physicians on St. Luke's Day, October 18.

In taking as his subject "The Influence of Harvey and his Contemporaries on Paediatrics," Sir LEONARD PARSONS said that there was nothing he could add to the known details of Harvey's life, nor would he attempt to prove that Harvey was a paediatrician. Nevertheless, Harvey and certain of his contemporaries by their contributions to the study of children in health and disease had helped to further paediatrics. Harvey lived in a time of enormous outpouring of intellectual energy. He saw the last years of Shakespeare and the rise of Milton. A scientific revolution was in progress which overthrew mediaeval authority. The chief agents in the revolution were Galileo, Descartes, and Bacon, all of them Harvey's contemporaries. The base of the scientific revolution was Padua, which was in the sixteenth and seventeenth centuries the most famous university in the world—

> ". . . the great desire I had
> To see fair Padua, nursery of the arts."
> (*Taming of the Shrew*)

It was from Padua, whose traditions had been carried on in this country by the Royal Society, that Harvey drew his inspiration.

Some idea of the state of paediatrics in the early part of the seventeenth century might be obtained from the writings of Shakespeare. Thus the mother of Coriolanus said to him: "Thy valiantness was mine; thou suck'dst it from me." Originally paediatrics formed part of obstetrics. The majority of children's diseases in the nineteenth and early part of the present century were, however, approached from the standpoint of the adult. It was true that a wide knowledge of general medicine was essential to the paediatrician, but the child was not an immature adult and required special study. When he (Sir Leonard Parsons) began the study of paediatrics at Great Ormond Street Hospital the number of babies admitted to the wards was extremely limited, and the great problems of infant morbidity and mortality were largely untouched. Within recent years it had been increasingly realized that mother and baby formed, before and after the birth, one biological unit. The trend was now towards the study of the premature child and the effect of antenatal conditions on the unborn and the newborn.

The close association of paediatrics with obstetrics had thus been again brought about. Paediatrics had returned to the position held in Harvey's day.

The Orator confessed that he found Harvey's *Exercitationes de Generatione* . . . (1651) obscure and difficult to understand. Harvey himself seemed to realize this, and invited his readers to weigh what he had put forward in the light of experiment. It had been said that the book revealed the last infirmity of noble minds, the degeneration of old age, but that was unjust, and indeed there were numerous similar observations on the formation of the foetus in his *De Motu Cordis* (1628). Within recent years authorities had studied *De Generatione* afresh and passed a new judgment on it. While *De Motu Cordis* was the crowning glory, *De Generatione* might have been Harvey's chief interest. In it he anticipated some ideas of the twentieth century, and he set his predecessors right on many points, such as the question of the placenta. Harvey said that Nature, like the painter, first sketched the outlines and then filled in the colour. It might be said of Harvey himself that he made the outline and the colour was filled in by his successors. If it was claimed that there was too much speculation in his work, speculation, after all, took its place as part of the scientific method. Observation and experiment were not methods initiated by Harvey; indeed, they were known to Galen, and at Padua Harvey learnt the importance of studying anatomy not from books but from dissections.

Of Harvey's contemporaries the orator spoke first of Francis Glisson (1597–1677), the first man of distinction to accept Harvey's work on the circulation. He discussed some of Glisson's important contributions to experimental physiology, and also his work on rickets (*De Rachitide*, 1650).

The history of rickets was a fascinating one. Almost nothing was heard of the disease until the seventeenth century, although it must have existed from the earliest times, especially in such areas as the Low Countries. There was in the National Gallery a picture dated 1490 which showed conclusive evidence of rickets in the subject. At the end of the sixteenth and beginning of the seventeenth century there was evidence that rickets was common, but Glisson spoke of it as an entirely new disease, originating some little while before the publication of his work in 1650. In 1655 James Cook, of Warwick, published his "supplementum" on the use of herb beer in the treatment of rickets. A book by Sir Thomas Browne, published posthumously in 1690, though written many years earlier, referred to many people who in childhood had suffered from rickets but afterwards became strong and active men.

Rickets was not mentioned in the London bills of mortality until 1634, but all the evidence suggested that it was prevalent in England before the seventeenth century, though first generally recognized between 1620 and 1630. With the drift of population to the towns and the industrial revolution, its incidence continued to increase, and except for the empirical discovery of the virtues of cod-liver oil at the beginning of the nineteenth century little was done about it until the work on fat-soluble vitamins. In 1928 the Orator had prophesied that by the middle of this century rickets would present no terrors—a prophecy which had come true. Exogenous rickets had been practically abolished in the United Kingdom, and the interest had now shifted to those endogenous forms which might arise through defect of renal function.

In his treatise Glisson referred to the theory that the disease might actually break out before the birth of the child. Maxwell's view was that foetal rickets did not occur unless the mother had osteomalacia. Another observation of the time was that scurvy might sometimes join with rickets, though it was not caused by that disease. It was remarkable that previously there had been so little mention of infantile scurvy, though full descriptions of the characteristics and cure of a disease of that name were given by writers in the middle of the sixteenth century. One explanation might be the change in the conception of scurvy. At that time a variety of disorders were included under the title of scurvy, but not the disease itself.

In 1642 James Cooke, who was in attendance on the Parliamentary army, obtained from the widow of Dr. Hall, of Stratford-on-Avon, certain of his observations on his treatment of scurvy and other conditions by herbs and drinks among other remedies, but the majority of the patients did not suffer from true scurvy. After Glisson's death infantile scurvy again lapsed into obscurity.

In the middle years of the seventeenth century John Mayow, of Oxford, made important contributions to paediatrics, chiefly connected with respiration. Eleven years after Harvey's death Mayow gave a description of the mechanics of respiration which might almost be accepted to-day, and he corrected Harvey in some respects. Mayow did not believe that the foetus breathed through the mouth, and he held that the placenta should no longer be regarded as a uterine liver, as Harvey regarded it, but as a uterine lung. The placenta at first did play a part as the uterine liver, and it was interesting that many years after Harvey's death Claude Bernard spoke of the placenta as the liver of the foetus. There was some suggestion that Mayow received credit for other people's work and was guilty of plagiarism, but it was significant that he was elected Fellow of the Royal Society four years after his last published work and on the proposition of Robert Hooke. He should be allowed some originality at least for his work on rickets, and in the Orator's view Mayow had been too harshly criticized.

Sir Thomas Browne, who was interested in various paediatric problems, said in his *Religio Medici* that we "are subject to the actions of the elements and the malice of diseases in that other world, the truest microcosm, the womb of our mother."

Coming to the last of Harvey's contemporaries, Thomas Sydenham, Sir Leonard Parsons said that Sydenham on the whole ignored the results obtained by experiments; he believed in observation at the bedside, and he had little in common with Harvey; it was doubtful, indeed, whether they ever met. Nevertheless, Sydenham might have been indebted to Harvey's experiments to a greater extent than he knew. Experiment was actually one form of observation, and clinical examination was a close-knit pattern of observation. Harvey had one great advantage over Sydenham—namely, that as a young man he had been to Padua and had come under the influence of Galileo. When Sydenham went to Montpellier he had already graduated at Oxford and by that time his ideas might have been somewhat fixed.

But the combination of the method of Harvey and of Sydenham had given to British medicine its greatest glory. Sydenham was the first to give a description of rheumatic fever, which he regarded as a fever in its own right and not a happening incidental to some other condition. He had almost been canonized as the patron saint of clinical medicine. Nevertheless his description of chorea did not compare with those given in the early years of this century, based on the same method of clinical observation. In his account of scarlet fever, which was said to be the first account of the disease under that name, he had failed to mention its most important manifestation—namely, sore throat. It was true that children might not complain of sore throat even when it existed, but Sydenham could not have examined the throat. It was encouraging to find chinks in the armour of this great man, because it made him seem more human.

Sir Leonard Parsons concluded with a picture of Harvey at the battle of Worcester, when he was said to be reading a book. He suggested from a little indirect evidence that the book was the Gospel of St. Luke, and he concluded by urging in that College which had found such inspiration in the work of Harvey that they should take to heart the words of St. Luke's great contemporary: "Seeing we are compassed about with so great a cloud of witnesses . . ."

BISSETT HAWKINS MEDAL

AWARDED TO SIR WILSON JAMESON

On the occasion of the Harveian Oration at the Royal College of Physicians on October 18, the Bissett Hawkins Medal was presented by the President, Dr. Russell Brain, to Sir Wilson Jameson, lately Chief Medical Officer to the Ministries of Health and Education. The medal is awarded by the College to a British medical practitioner who during the preceding ten years has done outstanding work in advancing sanitary science

or in the promotion of the public health. Sir Harold Boldero read the following citation:

"Sir William Wilson Jameson, G.B.E., K.C.B., M.D., F.R.C.P., retired from the post of Chief Medical Officer of the Ministries of Health and Education in May, 1950, having been concerned during his ten years' tenure of those offices with outstanding advances in the promotion and conservation of the public health.

"The impact of the second world war upon this country produced in unprecedented degree problems in hygienic control, in epidemiology, and in nutrition. Jameson was largely instrumental in setting on foot inquiries into those matters, and in organizing the measures of regulation and remedy which research had indicated as necessary. It will be remembered that he was appointed to these high offices after the Emergency Medical Service had been instituted; but the National Health Service Act was introduced during his tenure.

"There is no need to stress the measure of these great responsibilities. The mere recital of certain of the earlier concomitants of the war will be a sufficient reminder of the subsequent achievements of medical knowledge and sanitary organization—the conditions of life in air-raid shelters, the epidemiological problems arising therefrom, and the incidence of scabies.

"In the wider fields of practical epidemiology three major projects will always be associated with Jameson's name—the intensified attack upon diphtheria by immunization, the realistic approach to the control of venereal disease through contact-tracing and other social measures, and the institution of that survey of groups of the population particularly susceptible to respiratory tuberculosis, which is known as mass radiography.

"Another contribution in this same field, but of a somewhat different character, was the firm establishment under the Medical Research Council of a national Public Health Laboratory Service.

"Again, from 1940 onwards, Jameson, together with the committee of which he was chairman, was in great part responsible for advising the Government on nutritional policy, and for obtaining the introduction of those schemes under which the priority classes of expectant and nursing mothers, and children, were enabled to enjoy a dietary enlarged and sometimes fortified to meet their respective needs.

"In other directions also his enthusiasm and determination were influential in achieving results. The large-scale development of penicillin, the institution of streptomycin trials, and the introduction of B.C.G. all owed something to his efforts.

"To round out but not to complete the record, and to mark his interest in fields less related to the public health but nevertheless not so removed as to be disregarded, were his work on the Goodenough Committee and in the Councils of the World Health Organization. 'Nullum quod tetigit non ornavit.'"

BIOLOGICAL ASPECTS OF ATOMIC ENERGY

TWO-DAY CONFERENCE AT THE ROYAL INSTITUTION

A conference attended by over 500 scientific workers was held at the Royal Institution, London, on October 20 and 21 under the auspices of the Institute of Biology and the Atomic Scientists Association, with the support of the British Association. The chairmen of the four sessions were Sir HENRY DALE, O.M., F.R.S., Sir JOHN D. COCKCROFT, F.R.S., Sir ERNEST ROCK CARLING, and Lord BOYD-ORR, F.R.S., and the discussions ranged over biological and medical effects of nuclear radiations, tolerance levels and measures of protection, genetical hazards, and the future of atomic energy. The proceedings were private, but the Press were invited to a conference with the chairmen and authors after each session.

The Responsibility of Scientists

Lord BOYD-ORR, at the final session, said that the new powers which were being revealed by physics and biology might be used either to usher in a new golden age or to devastate the world. In view of this tremendous issue, some scientists, among whom he ranged himself, felt that science should be completely free and independent. Frank statements should be made to the public about what could be done, and thus world-wide public opinion might be created among the common people of all countries, including those behind the Iron Curtain, which would direct science towards beneficial ends. The public, which was going either to suffer or to benefit, ought to be allowed to form its own judgment. Everybody, Lord Boyd-Orr continued, was scared by the thought of the atom bomb, but it was the biological side, to his mind, which was now more important.

Professor C. A. COULSON, F.R.S., said that the issues with which scientists were now confronted were not merely scientific but moral. The scientific movement, at least in the West, had been founded on certain basic convictions—integrity, respect for the opinions of others, standards of personal judgment, and a sense of responsibility not only for the publication of work but for the foreseeable consequences of it. The scientist was not just a scientist, he was also the guardian of some of the most precious values of civilization. He hated secrecy and would take no part in it. Scientists would be untrue to their convictions if they allowed moral obligation to be forfeited.

Professor KATHLEEN LONSDALE, F.R.S., also spoke of the unfortunate effects of secrecy. This was illustrated, she said, by an effort which she and others had made recently to find out what were the health hazards in uranium mining and what protection was afforded to the workers. Every possible source had been consulted in vain. The only information available related to the period 1930–9 in Czechoslovakia, which showed that the number of deaths from lung tumours in uranium mines among men above the age of 35 was thirty times that of the ordinary male population of Vienna. A similar high incidence of liver tumours was found among native miners in gold mines in South Africa, where almost certainly there was deleterious radioactivity.

Radiation and Heredity

In the session on the biological implications of atomic energy Sir ERNEST ROCK CARLING said that the various papers had emphasized what had been known for a long time, that all effects of radiation on heredity were harmful. Dr. C. D. DARLINGTON, F.R.S., while acknowledging that the occurrence of mutations in plants and animals had been the basis of evolutionary change, said that after exposure to ionizing radiations the rate of mutation was multiplied so that a far greater number of misfits were produced. Dr. D. G. CATCHESIDE pointed out that these effects had been studied in organisms as diverse as *Drosophila* (in which the phenomenon of *x*-ray-induced mutation had been discovered), moulds, fungi, bacteria, green plants, and mice. All that could be done from the point of view of predicting the effect on human beings was to extrapolate what was known in other organisms.

Control of Hazards

Dr. E. E. POCHIN addressed the conference on the control of hazards in the clinical use of radioactive iodine. In ordinary use in hospitals, he said, any hazard could be successfully met by the protective measures available. Such protection for the patient and those with whom he came in contact was rather a matter of scrupulous attention to detail than the application of any difficult or complicated methods. Hazards, at least with radioactive iodine, were not difficult to control, though there were other elements not at present used on account of their hazards.

Dr. JANET VAUGHAN, who with other workers from the University of Oxford produced a paper on hazards arising from radiostrontium, based on experiments with rabbits, emphasized the need for exact statement in all work on radiation. It should clearly be stated in dealing with isotopes what animal was used, its age, its diet, and so forth. In other words, it must not be assumed that the same effects would be seen in the young as in the old, or in the well-nourished as in the ill-fed. Standardization of working conditions was important, or at least a statement of what the conditions were.

SOCIETY OF MEDICAL OFFICERS OF HEALTH

PRESIDENTIAL ADDRESS BY DR. J. M. GIBSON

At a meeting of the Society of Medical Officers of Health at B.M.A. House on October 19 Dr. J. M. GIBSON, of Huddersfield, was installed as president of the society for the year 1950–1. In his presidential address, entitled "Give Us the Tools," Dr. Gibson dealt with the difficulties and frustrations of medical officers of health since the inception of the National Health Service.

Administrative Responsibilities

Dr. Gibson prefaced his address by stating what he felt would be undisputed, that the most urgent need in the field of public health was for the erection of more up-to-date houses to combat the evils of present-day overcrowding. He could not cover all aspects of public health, and so proposed to concentrate on the most outstanding difficulties encountered since the National Health Service Act of 1946 came into operation. The greatest good to the greatest number could be achieved only when all branches of medicine were working together in harmony, and it was nothing short of a tragedy that the Act had completely failed to secure this. There was urgent need for medical officers of health to be restored to their former position of close administrative and clinical touch with the hospitals in their areas. It had been said that a wise lay administrator concerned himself with the business side of administration and that in dealing with medical matters he relied upon the advice given by his medical advisory committee. But, when all the experts had submitted their proposals for new expenditure, who could be expected to hold a fair balance? Not one of the specialists themselves, not the lay administrator—for he could not assess the urgency of any particular proposal—and certainly not the chairman of the house committee. The medical officer of health, if he was to perform his duties satisfactorily, could not remain divorced from hospital work. His voice must be heard not only at house committee meetings and hospital management committee meetings, but also on hospital boards. The Minister of Health had mentioned on several occasions that he regarded the medical officer of health as the connecting link between the three administrative bodies responsible for the Health Services—the local health authority, the executive council, and the hospital board—and it had been thought at first that medical officers of health could exercise this function with the hospital board by means of a liaison committee. Experience had shown that this arrangement was unworkable, and it was essential that the medical officer of health should be represented on the committees at all levels.

Isolation Hospitals and Sanatoria

The medical officer of health must be given the fullest measure of responsibility in the management of the isolation hospital. The most important role of these hospitals was still in the prevention of disease, and for this the medical officer of health of a district was the only person who could say what particular case should, or should not, be admitted to the isolation hospitals.

Next in importance to the isolation hospital came the sanatorium. The medical officer of health was not so much concerned here with the clinical side, but, since isolation of infectious cases played such an important part in reducing the incidence of tuberculosis, he could not allow the admission and discharge of patients to and from sanatoria to be placed in other hands without protest. Another type of hospital over which medical officers of health wished to retain some measure of control was the maternity home. These had not been regarded as hospitals in the past. They had been erected by local authorities so that mothers at the time of their confinement could have better facilities than were available in their own homes; cases in which difficulty could be foreseen were not as a rule admitted to maternity homes but dealt with in hospitals. The medical officer of health, from his intimate knowledge of the home circumstances of patients, was in the best position for deciding what priority should be given to applicants for admission to maternity homes.

Care of Children

Another effect of the National Health Service Act which was causing anxiety was the tendency to remove the specialist examination and treatment of school-children from school clinics to hospital precincts. This change had not been widely applied up to date mainly because the out-patient accommodation available at hospitals was already taxed to its utmost capacity, but the policy was there and must be resisted.

Dr. Gibson then reviewed the effects of three new legislative measures which had a direct bearing on the work of the medical officer of health—namely, the National Assistance Act, 1948; the Children Act, 1948; and the Milk and Dairies Regulations, 1949.

With regard to the first, the president ended his analysis by affirming that in the interests of economy and efficiency all social services for the sick, aged, and the handicapped, and for the prevention of illness and the provision of aftercare, should be co-ordinated through the health department. The same applied, though perhaps with even greater force, to the care of deprived children. In the panicky legislation which had followed the publication of the Curtis Report, responsibility for the care of these children had been transferred by the Children Act from the Ministry of Health to the Home Office, from maternity and child-welfare committees of local authorities to children's committees, and, in most cases, from the medical officer of health to a newly appointed officer, the children's officer.

The care of deprived children was so much a medical problem, and the children themselves were so often problem children, that in their interests the work should be closely linked with the work of child welfare generally and of the school health service. This could be done only through the medical officer of health's department. A children's officer could do much to help these children, but she should operate as a member of a team in the health department, being assisted by the health visitors and school nurses.

Cleanliness of Milk

The president then referred to the Milk and Dairies Regulations, 1949, which had transferred the supervision of the production and handling of milk at the farm from the Ministry of Health to the Ministry of Agriculture and Fisheries, and so from the staff of the health department to officials of the newly formed milk and dairies committees. Local authorities were still responsible for the supervision of all sanitary matters affecting the farmer's residence, and it was their duty to see that the farmer and his family had a satisfactory water supply, but they were no longer concerned with the condition of the shippons or of the purity of the water used in the dairy. In the past, sanitary inspectors had succeeded in many areas in raising considerably the standard of cleanliness of milk supplies by visiting farms and giving advice on the spot. Now they were debarred from this service and no one else appeared to be doing it.

Milk was a most important article of diet, particularly for the young, and of all foodstuffs was probably the most subject to contamination by pathogenic bacteria. The Food and Drugs Act, 1938, gave very wide powers to the public-health staff to supervise the preparation and storage of all food for sale. It was strange, then, that milk had been singled out by the new regulations as the one article to be removed from this supervision, just at the very point in the course of its handling where contamination was likely to occur.

In concluding his address, Dr. Gibson mentioned two further "wants" of medical officers of health. They desired for their preventive work to be linked more closely with the industrial medical services.

Lastly, there was the question of increased remuneration. They had submitted claims which they thought were reasonable, taking into account the training and qualifications necessary for medical officers of health and bearing in mind the salaries obtainable in other medical fields. Believing in the justice of these claims, they must await with every confidence the decision of the arbitration tribunal now considering the matter.

Correspondence

Useless Routine Medical Examinations

Sir,—I have read with much interest the recent Dawson Williams lecture by Professor Alan Moncrieff (October 7, p. 795). In his lecture Professor Moncrieff, *inter alia*, criticizes the system of medical inspection of school-children employed in this country for the past 42 years, and makes suggestions for its improvement. As one who has been engaged in school medical work for nearly the whole of that period, and indeed for two years before medical inspection became compulsory, I should like to say that I largely agree with his remarks on the subject as well as with your editorial comments. I have long been impressed with the wastage of man-power and money involved in carrying out the present system, and I heartily support Professor Moncrieff in his plea for a drastic change.

The present procedure is far too rigid, and involves far too much time in detailed examination of normal children and filling up record cards with bare negatives. To add to the doctor's and nurse's clerical work, the Ministry of Education has issued a new record card, replacing the simpler but sufficient record cards of many local authorities. I am told that this card was drawn up by a committee of experts, and it certainly has every appearance of having been designed by a committee. And along with this extraordinary card is a large graph card on which to record heights and weights, instead of simply writing the figures down. Here again more time is wasted and not seldom a good deal of exasperation experienced. And all that the finished card will generally show is three or four dots for height and three or four dots for weight, with intervals of years between them, and meaning simply nothing. One might very well go further and ask whether the weighing and measuring of all children are themselves really necessary. There are tall and short children, heavy and light children in any age group, and all may be equally normal. Certainly weigh the children that need weighing, and weigh them sufficiently often to make the figures significant, but I am convinced that this wholesale weighing is quite unnecessary. This and a lot more could be scrapped without loss of efficiency and probably with gain, even though many nice statistical tables will disappear from the school doctor's reports. It may be desirable to retain a routine inspection for school entrants, but after that the "screening" system mentioned by Professor Moncrieff would suffice and allow more time to be devoted to the children who really need medical investigation. In support of this, may I give an early experience of my own? As I mentioned above, I carried out school medical work for the two years prior to 1908. I had been appointed M.O.H. to a Yorkshire town in 1903, and, keen to extend my sphere of work, I prevailed on the education committee to appoint me their school medical officer in 1905. I had to devise my own system of inspection of the school-children, and as I had no nurse to assist me I sought the co-operation and help of the school teachers. They responded extraordinarily well, and to make their help as efficient as possible I gave them a course of lectures on the health of school-children and on school hygiene. The surprising thing was that most of the teachers attended these lectures, and most of them became enthusiastic coadjutors in this new work. I also got a leaflet printed summarizing the main points in my talks, and had these distributed among the teachers. I visited each school as often as I could, and first of all I examined any children picked out by the teachers as possibly having some physical or mental defect. I then had a general look over the children doing their class work, and finally I had them marched slowly past me. By this apparently cursory inspection, I was able to detect many children who, *prima facie*, called for a detailed medical examination, which I did then or later. In the case of those requiring treatment, advisory notes were sent to the parents, but, seeing that there was no school clinic and private medical treatment had to be paid for, the results were somewhat meagre. But, with the knowledge resulting from these inspections, the teachers were often able to help the children in school. It was something to know which out of a group of backward children was deaf, which had bad eyesight, and which was mentally defective. However, the point I want to make here is that by this simple procedure a remarkably high degree of ascertainment was achieved, as I was able to check later when the official routine system came into force. My experience here also indicates that in any system of "screening" the assistance of the teachers would be of the very first importance.—I am, etc.,

Langport, Somerset. Thomas Gibson.

Child Health and the Future

Sir,—As administrators we must be grateful to Professor A. Moncrieff (October 7, p. 795) for demonstrating some of our shortcomings, such as hesitancy in health education and our lack of initiative in prevention of tuberculosis in infant-welfare centres. What might, however, be called logistics does enter into some of his suggestions, such as the one that infant-welfare centres should be conducted by the family doctor.

In Ilford we have 15 such centres per week, and there are approximately 75 general practitioners. If 15 doctors are chosen to do these centres the other 60 will be just as badly off as they are now, except that the centres will be run by their competitors. If each doctor is given a chance, a different one will be in attendance at any one clinic each week, to the great detriment of the mother and child, who will have no continuity of treatment. Perhaps it is suggested that we run 75 clinics a week, one for each doctor, but then the ratepayers will have something to say, and the staffing problem would be intolerable.

Perhaps, however, the idea is that the practitioners do this work in their present surgeries. In most cities this will mean collecting children in overcrowded premises with full opportunities for cross-infection, or even a wait in a queue outside, maybe in the rain—that is, if the doctor concerned encourages mothers to bring their healthy babies. No doubt the idea will be practicable when there are enough doctors, adequately imbued with the idea of prevention, to serve the community, and when they work in adequately staffed and equipped health centres. However, then, Sir, there will be no need for administrative action as suggested by Professor Moncrieff, for mothers will, of their own accord, prefer their family practitioner to local authority centres. These centres exist only because they meet a need which cannot otherwise be satisfied.

With respect to the suggestion that nurses and teachers pick out children for reference to a doctor in lieu of routine medical inspections, I would like to know the proportion of cases of nocturnal enuresis, cryptorchidism, tinea pedis and cruris, constipation, haemorrhoids, and menstrual difficulties that will be disclosed by such methods. This point is, however, not as important as the fundamental ignorance of most of us, including doctors, about what is a disorder. Almost all of us suffer from physical imperfections, and it is the most difficult task in medicine to decide which of these imperfections are of significance and which not, and our teachers have not helped us much in the past. I refer to enlarged tonsils, knock-knees, flat feet, constipation, etc., that vast border-line between health and disease. To decide this problem is the most delicate task that that can be required of a doctor, and it must be decided in the vast mass of school-children and not in a few selected by teachers and nurses.

In our natural revolt against too frequent and unnecessary inspections, such as twice a year or yearly, we must not go to the other extreme and have no routine examinations at all.—I am, etc.,

Ilford. I. Gordon.

Sir,—Professor A. Moncrieff in his stimulating article (October 7, p. 795) decries the waste of medical man-power in routine medical inspections of schools. This system does, however, afford the school doctor the opportunity of spreading health education to large numbers of mothers, who are willing in many cases to sacrifice half a day's work with pay to attend these sessions. Many problems which the mother would hesitate to place before her overworked general practitioner are discussed at leisure with the school doctor. Surely this is an ideal

method of educating the child, through the mother, in matters of health hygiene or sex, and may possibly be of more value than direct teaching in schools. It is doubtful whether a nurse, however competent, has the authority or breadth of outlook to fulfil this function.

The present system of school medical inspections also provides a competitive stimulus which is of some value in maintaining a standard of cleanliness.

"In New York . . . where only entrants now have a complete examination" the problem is somewhat different. In America there is a widespread preoccupation with matters of health and disease, and almost too great a wealth of popular literature devoted to medical matters. Social standards are also considerably higher than in Britain. It would be untimely to terminate routine inspections among the poorer sections of the community at least—even though they be monotonous—until our social conditions improve.—I am, etc.,

London, N.4. CECILIA GALTON.

Safety in Prams

SIR,—Mr. D. L. Davies's somewhat disingenuous letter (October 14, p. 889) suggests that mothers who buy a pram which they would imagine should, at present prices, be complete should then take the pram to a member of his association to have it altered in order to make it safe. My baby, who is as active as any other baby of nearly a year, has now tipped a variety of prams backwards and has had at least three serious falls. I have never attached the side-pieces of a harness to the side-pieces on the pram; the fault has always lain in the initial position of the fixed side straps, whose ends when stretched straight out forwards are barely within the wheelbase. It seems wholly unreasonable to expect the mother to go to the trouble and expense of having the straps removed and replaced. Is it quite impossible for the manufacturers to place the straps in a safe position in the first instance, or, better, to arrange that the straps can be put in different positions for babies of different ages and activities?

Another point which Mr. Davies does not cover is that in these days when very few mothers have nannies to wheel babies morning and afternoon the pram is increasingly needed as a safe container in which to leave the baby in the fresh air. The springing of prams continues to be adjusted primarily to ease pushing, and not to maintain safety. I should like to add that I hope a fellow-suffering mother will be a member of the committee that I understand the Royal Society for the Prevention of Accidents is considering setting up.—I am, etc.,

London, W.6. JOAN MARSH.

Safety on Cycles

SIR,—Every country doctor sees from time to time a frightened mother carrying into his surgery a no less frightened child suffering from a badly bruised ankle and lacerated foot. At such times one wonders when some enterprising manufacturer of pedal-cycle accessories will prevent children who are being conveyed on carrier-seats from catching their feet between the bicycle's rear wheel spokes. All that is required is a pair of simple metal shields to bolt on between the back stays. The potential market for such a product must, in rural areas, be very great, and appears to be untapped.

It is to be hoped that someone in the cycle trade will devote the same thought and attention to this problem as Mr. D. L. Davies in his letter (October 14, p. 890) so obviously has to the prevention of accidents to children in prams.—I am, etc.,

Mattishall, Norfolk. CHARLES S. THOMSON.

Acute Liver Disease

SIR,—I have read with interest the article of Dr. A. L. Latner entitled "Regime for the Treatment of Severe and Acute Liver Disease" (*Journal*, September 30, p. 748) in which he treated five cases of hepatic coma with glucose, vitamin supplements, and plasma. Four cases recovered and the fifth showed marked temporary improvement. I feel that this series is too small to warrant his conclusion that this satisfactory outcome is a direct result of therapy. As long ago as 1879, Mossé described six cases of "ictère grave" with four recoveries and attributed these results, at least in part, to a therapeutic regime of milk, quinine, and julep.

We have for some time been treating acute liver coma by a method very similar to that described by Dr. Latner; the principal difference being that somewhat larger doses of plasma were administered than in Dr. Latner's series. While nine cases died, the diagnosis of massive hepatic necrosis being confirmed in all histologically, a further two cases who received treatment that was little more than symptomatic both recovered. One was in coma for five days, the other for a week.

I feel therefore that, with the possible exception of the use of "aureomycin" in these cases as described by Farquhar and others (1950), there is still no satisfactory therapy for hepatic coma.—I am, etc.,

London, W.C.1. J. M. WALSHE.

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Abnormalities in Developing Chickens

SIR,—I read with great interest Mr. W. P. Blount's letter in the *Journal* (September 30, p. 785). Mr. T. Barton Mann, of the biological research laboratory of Messrs. J. Bibby and Sons, Ltd., Wirral, reassures me that the riboflavin and manganese contents of the eggs supplied for my experiments were known to be adequate from routine testing at regular intervals. Riboflavin was tested by the method described by Mr. Mann himself in *Analyst*, 1946, **71**, 166, and manganese was estimated spectrographically.

In view of the very nature of my experiments it is perhaps superfluous to point out that special care was taken throughout to ensure that eggs were taken from flocks not showing any similar abnormalities, and due attention was paid to eliminate as far as possible known teratogenous factors such as fluctuations of temperature during incubation. Physical conditions of incubation may be accepted as satisfactory, as hatches averaged 85% of fertile "uninjected" eggs. In every experiment an equal number of control eggs were put in the same incubator in which insulin-treated eggs were incubated.

As I have mentioned in my article on insulin-induced skeletal abnormalities in developing chickens (*Journal*, August 12, p. 386), both the incidence and severity of the deformities increased with the dose of insulin—e.g., the occurrence of limb deformities resulting from injection of 2.5 units of insulin on the fifth day of incubation was 46%, whereas with 5 units of insulin, injected also on the fifth day, it rose to 85%. I would be very interested to know if Mr. Blount noticed such a high percentage of abnormalities among the "so-called normal embryos" he has examined, and, again, if those abnormalities presented the same radiological and histological features as I have described in the case of insulin-induced deformities. As Landauer has pointed out on page 97 of the Storrs Agricultural Experiment Station *Bulletin No. 236* (referred to by Mr. Blount in his letter), the term "chondrodystrophy" (achondroplasia) has often been loosely applied in poultry science to different pathological conditions without histological confirmation, and *not* to a single clinical and pathological entity, as in medicine. In any case, if Mr. Blount believes that the deformities he had observed were linked with nutritional deficiencies—e.g., of riboflavin and other members of the vitamin-B complex, I am indeed gratified to note that he lends further support to my statement: "One can therefore anticipate that deficiency of phosphorylating enzymes, produced by lack of vitamin-B complex, may induce malformations in the same way as insulin hypoglycaemia can, by causing disturbances to cellular carbohydrate metabolism at critical periods during development" (*Journal*, August 12, p. 389).

I have read the two books suggested by Mr. Blount—viz., Storrs Agricultural Experiment Station *Bulletin No. 236*, on "Hatchability and Environment," and Mr. W. Marshall's paper to the Eighth World Poultry Congress, entitled "The Relationship of *Visceral* Anomalies of Full-term, Dead-in-Shell to

Embryonic Malposition" (my italics), which, though interesting in itself, seems, to me at any rate, irrelevant in the present context.

Finally, I am not at all sure if the congenital anomalies induced by rubella during pregnancy are the result of "fluctuations of temperature," presumably caused by pyrexia during the infection, as has been naively suggested by Mr. Blount. As far as I know, it has not been clearly demonstrated that other febrile conditions during pregnancy, apart from rubella, can give rise to congenital defects in the foetus.—I am, etc.,

Liverpool. P. K. DURAISWAMI.

Modification of Boyle's Apparatus

SIR,—In reply to Dr. D. Zuck's letter (*Journal*, September 30, p. 787) I would state that the principle of using the patient's breath plus basal oxygen for induction of anaesthesia demands the arrangements found in the special absorbers. I have always tried to reduce to a minimum the weight and bulk of my own apparatus, as so much of my practice has called for portability. The principle of the modification described is induction by the established method of N_2O and O_2, which evaporate the ether to full anaesthesia. CO_2 absorption is then used and maintained by the necessary oxygen, with small accessions of ether as required. There is no claim other than this. The difficult case still arises, but this is now often met by muscle relaxants and the use of the newer methyl-N-propyl ether, which is so much less irritating and is suitable for CO_2 absorption.—I am, etc.,

Glasgow, C.3. W. B. PRIMROSE.

SIR,—The criticism by Dr. D. Zuck (*Journal*, September 30, p. 787) of Dr. W. B. Primrose's account of his modified Boyle's apparatus (September 16, p. 676) is a very fair one. He makes no suggestion, however, on how the question of ether vaporization may be overcome. Dr. Primrose in his account utilizes the ether bottle as an absorber, the chloroform or "trilene" bottle being by-passed when the circle absorber is in use. If, however, the positions of the chloroform and soda-lime bottles be transposed, then by putting ether into the second bottle a simple "draw-over" vaporizer can be incorporated into the circuit on the inspiratory side of the absorber. The concentration of ether achieved with this type of vaporizer would not be as high as when baffles or wicks are incorporated, but would nevertheless be considerably in excess of any concentration which could be obtained where the only vehicle available is the basal oxygen flow. It would, in all probability, be necessary to enlarge both the inlet and the outlet apertures to this ether vaporizer in order to reduce the resistance to inspiration, but this should not prove to be an insuperable difficulty.—I am, etc.,

Coventry. JAMES MCNAUGHT INGLIS.

SIR,—Dr. W. B. Primrose has described (September 16, p. 676) a most ingenious way to convert a standard Boyle's machine into a closed circuit system and is to be congratulated on the simplicity of the modification. I cannot but feel, however, that the weak spot is the glass bottle for the soda lime. I am sure that in general use this will get broken more readily than previously because of the tube entering from below. Surely it would be simple to have an adaptor to screw on to the top of a standard M.I.E. absorber, which could then be screwed into the normal position for the bottle. The whole apparatus could thus be modified by the owner who has bought the necessary parts.

Dr. D. Zuck (September 30, p. 787) rightly pointed out that the strength of ether vaporized will be low when using the closed circuit. In times when curare is given to produce relaxation I would have thought that deep ether was no longer used for this purpose, or alternatively that those who used deep ether would not also be using a closed circuit system. Ether in an open circuit bottle is a useful adjunct to intravenous medicaments when only using the basal flow of gases: I frequently do this myself and the setting is usually at minimum.—I am, etc.,

Southsea, Hants. H. B. C. SANDIFORD.

Treatment of Pink Disease

SIR,—The article by Professor W. S. Craig (*Journal*, September 30, p. 773) on this disease, which through its long duration can be most exasperating and tantalizing for both patients and doctors alike, will be most welcome to all general practitioners in this country. I would, however, like to add a point of interest.

In an article of the January edition (1950) of the *Medical Journal of Australia*, Dr. Donald B. Cheek makes a most interesting and possibly revolutionary contribution to the treatment of this disease. Supported by clinical and biochemical investigations he found in babies and young children a depletion of NaCl in the blood serum (which partly accounts for most stubborn attacks of diarrhoea) and a lowered activity of the suprarenal cortex. The treatment he accordingly suggests is two teaspoonfuls of salt (NaCl) per day until improvement occurs, and in more severe cases additional injections of desoxycorticosterone, 5 mg. for four days. His results with this therapy appear to be most successful and certainly worth a trial.—I am, etc.,

Spennymoor, Co. Durham. E. BRAUER.

Observations on Cervical Erosion

SIR,—I was particularly interested in Dr. Jean R. W. Ross's article (September 16, p. 647), for I have recently re-examined 94 patients previously suffering from cervicitis and erosion and treated by dilatation and cautery, or dilatation and "conization" of the cervix during the past five years in the Nuffield Department of Obstetrics and Gynaecology, Radcliffe Infirmary, Oxford. Unlike Dr. Ross, I have not included puerperal patients, for I have been able to show that many erosions seen within three months of delivery are "involuting" erosions which heal without treatment. Undoubtedly, the inclusion of cases of this nature partly explains the cure rate of 4.7% achieved by cautery without concomitant dilatation of the cervix reported by her. She describes 109 parous patients suffering from abdominal pain (60%), menorrhagia (19%), leucorrhoea (80%), dyspareunia (9%), frequency (25%), and dysmenorrhoea (11%), and ascribes these symptoms to the presence of a cervical erosion. This apparently reduces the problem of treatment to the simple remedy of cauterizing the epithelium of the lower cervical canal and erosion with electric thermo-cautery.

I submit that many of the cases described were suffering from "cervicitis," of which an erosion may or may not be an outward manifestation; and it is my belief that it is illogical to treat a mere solitary sign (an erosion) and some of the symptoms, and yet ignore the remainder of the pathology in these patients. The procedure of preliminary dilatation of the cervical canal to promote drainage of the glands is as important as the subsequent cautery, and moreover it prevents the complication of cervical stenosis and haematometra which marred the results in 1.9% of the patients.

It has been my experience, substantiated by analysed results, that the more severe cases associated with hypertrophy of the cervix are better treated by dilatation and "conization" of the cervix. Even with this treatment recalcitrant cases occur in which only hysterectomy (abdominal or vaginal) can cure. Inspection of cervices previously treated unsuccessfully by local measures and subsequently removed by hysterectomy has impressed me with the frequency with which the external os appears relatively normal, but numerous nabothian follicles are seen extending up the cervix as high as the level of the internal os.—I am, etc.,

Oxford. DERK CRICHTON.

Medical Students in Prague

SIR,—I was most interested to read P. L. C. Diggory's article (September 30, p. 780). Having been a medical student in Prague myself and having returned to that town for several months after World War II, I admire how much and how correctly Mr. Diggory has seen. There is, however, one important point with which I must disagree and which I think will be of some interest. Mr. Diggory says he admires the close and cordial relations existing between the medical staffs of Czech hospitals. Even the humblest laundry maid was regarded, and regarded herself as, an integral member of the hospital

team, and was assured that her opinions and suggestions would be welcomed at regular meetings where all of the staff were present. I wonder what Mr. Diggory's opinion would have been had he been present with me at one of these staff meetings in a Czech general hospital in the winter of 1946? In this "democratic" circle the hospital porter happened to be the chairman, or president as it was called, and all the laundry maids and other maids were present just as Mr. Diggory mentions, and had their say. In that particular hospital, visiting hours happened to be every day. I proposed that there should be a reduction in visiting days, and suggested that on the two operating days there ought to be no visits, as patients who had just been operated upon ought not to be disturbed and drips and transfusions, etc., had to be fixed. The laundry maids were all for it—I mean for reduction of visiting hours—the chairman, the porter, was against, and my proposed change fell through. It was afterwards explained to me by the superintendent that the maids were in favour of reduction of visiting hours because they would have less cleaning to do through less dirt being carried into the wards and corridors by the visitors. The porter was against reduction because that would have meant for him reduction in tips. Needless to say, the lady in charge of the cloakroom was also against. I wonder which institution is the more democratic one, the one just described or the one in which doctors do not have to explain the necessity of intravenous drips to laundry maids, just as these do not have to justify to the doctors their washing technique?—I am, etc.,

Billingham, Co. Durham. J. Abels.

Smoking and Carcinoma of the Lung

Sir,—I should like to comment on certain points raised in this most interesting and important communication (*Journal*, September 30, p. 739). A possible explanation of the finding that the increase in deaths from carcinoma of the lung during the past 25 years is greater than the increase in tobacco consumption is that the number of *heavy* smokers may have increased much more during this period than the increase in tobacco consumption would suggest. There has certainly been a remarkable increase in very light smokers—women. I suspect, however, that there has also been a steady increase in the smoking of men. Twenty-five years ago anyone who smoked 20 cigarettes a day was regarded as a heavy smoker. To-day he is just an ordinary smoker.

In 1936–7 I investigated the smoking of a random sample of 804 males in a wage-earning urban community. There were 445 "heavy smokers"—smokers of 10 or more cigarettes per day—i.e., 55%.[1] If we compare this with Table V of the present investigation, which showed the most recent amount of tobacco smoked regularly by 622 male control patients, and assume that half the smokers of 5 to 15 cigarettes per day smoked 10 to 15, we find that 68% were "heavy smokers" according to my definition, an increase of 13% in 11 years.

With regard to the anomalous finding that there was no distinct association between inhaling and the development of carcinoma of the lung, the suspicion mentioned by the investigators—viz., that patients might not have been aware of what is meant by inhaling—is probably well founded. Many smokers, including doctors, I have found did not understand the term. I have often required a patient to light up to settle the matter and have often found that patients who thought they were inhalers were mistaken. The most useful check is to ascertain whether or not the smoker retains the cigarette between his lips during most of the smoke. If he does, he is almost certainly not an inhaler.

I take the investigators to task for their 36 references to the habit factor in smoking whilst completely ignoring the much more important craving factor. Both craving and habit are of course subjective and cannot therefore be measured. The fact, however, that satisfaction can be obtained from administering tobacco in ways other than by smoking—by chewing and snuffing, and also by the administration of nicotine by various routes[2]—shows that it is the action of the tobacco that matters and not the actions associated with its administration, which become largely habitual. If the carrying out of habitual actions were all-important, as calling smoking a habit implies, this could be done without lighting the tobacco, at great saving to the habitué but with virtually no satisfaction. It is clearly therefore a violent euphemism to refer to smoking as a habit. Tobacco smoking is a drug addiction (to be quite precise, a means of administering a drug of addiction, nicotine), and the drug addictions are specific diseases—specific intermittent intoxications. Nicotinism is clearly no less a specific disease than, say, plumbism, although addicts are, for obvious reasons, much more at pains to conceal their symptoms. Since tobacco smoking is a disease and a preventable one, it is our plain duty to prevent it.

The possibility that not only the interviewers but the investigators themselves may have been biased by their own smoking does not appear to have been taken into account. The fact that such harsh words as drug-craving, drug addict, drug intoxication or addiction, etc., have been scrupulously avoided suggests, to my mind, that the investigators are addicted to tobacco. (I may say that I do not know and have not tried to ascertain whether this is so or not.) Smokers, I have observed, often speak of smoking matters with an air of judicial detachment, yet it has often been obvious to me, an ex-inhaler of tobacco smoke, that their expressions of opinion on such matters were profoundly influenced by their craving for the drug. What is craving but "a fervent wish" (*O.E.D.*), and it cannot be doubted that such a wish often fathers thoughts on smoking matters. Admittedly non-smokers may be prejudiced against smoking, but just as non-addicts of morphine usually take a detached view of that affection and are far better able to do so than addicts, so also, in my view, can non-addicts of tobacco.—I am, etc.,

Wallasey. Lennox Johnston.

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1 Johnston, L., *British Medical Journal*, 1945, **2**, 98.
2 —— *Lancet*, 1942, **2**, 742.

A Secret Remedy for Cancer

Sir,—There are many points at issue between *Picture Post* and the *British Medical Journal*, but there is none which is not best answered by the action of the Minister of Health in setting up the independent committee of inquiry for which we asked. But there is one point on which Mr. Rees Evans deserves to have his case made clear, once again. For no less than 26 years Mr. Rees Evans's offer has in fact been open under the conditions now accepted. He always felt that he should submit his treatment to this type of investigation in order that it might, if approved, be backed by some greater authority than his own. This is the first time that any such inquiry has been offered.—I am, etc.,

London, E.C.4. Derek Wragge Morley.

*** Mr. Rees Evans has agreed to submit to a Ministry of Health Committee "whatever they may ask concerning my materials and methods." Twenty-seven years ago (Mr. Morley has chosen the figure 26 with care) he refused to disclose the constituents of his secret remedy to an earlier cancer committee of the Ministry of Health.—Ed., *B.M.J.*

Johann Mikulicz-Radecki

Sir,—I feel sure that no one will be more interested in the story of Mikulicz-Radecki than my friend Sir Gordon Gordon-Taylor, and those of us who are inquiring about the history of our art must be grateful to Dr. S. Galewski (September 9, p. 630; see also October 7, p. 839) for his vivid picture of the life-story of Mikulicz. I have to confess that ever since I knew anything about Mikulicz I have regarded him as a German and have always heard him spoken of as belonging to the old regime in that country. There is no doubt that he was at least of the German school and that his surgical upbringing was in that tradition. Whatever his country of origin he was universally recognized as a great surgeon, and the respect and esteem in which he was held during his lifetime continue to the present day. Surely mere country of origin had little to do with his reputation as an outstanding figure or his position in the surgical world.

When I first visited Vienna in 1899 many of the leaders there were nationals of some other country than Austria, but so far as

surgery was concerned they belonged to the Viennese School. So it certainly was in 1906 when I first visited the United States, and so it is to-day where many notable men who have added to the lustre of American surgical achievement were natives of other lands. Names like Christian Fenger, Albert Ochsner, the brothers Beck, Willy Meyer, and hosts of others at once come to mind, and so it is undoubtedly in other countries. Surely what really counts is not nationality or even knowledge and skill in surgery but those things which go to make leaders and above all else character and conduct. These attributes were present in a marked degree in Mikulicz, and, although I never had the privilege of meeting him in person or of seeing him operate, I feel I have an intimate knowledge of his work, because throughout the whole of my surgical career I have always heard so much of his characteristics and often at first hand from those who had been associated with him, like the late Professor Archibald Young, of Glasgow. He seems to have made a great impression on all who worked about him. Lord Moynihan stated that in 1903 Mikulicz told him that he had operated upon 35 cases of perforated gastric ulcer with 34 deaths as evidence of his conviction that it was the duty of the surgeon confronted with this catastrophe to give the patient the chance that only operation provided. There is also the quite touching story of his last illness and the way he faced the inevitable.

In a profession like ours nationality counts less than deeper things, and that truism is expressed in the simple motto "Without Frontiers" adopted by the Moynihan Club, that association of travelling surgeons which was started by the late Lord Moynihan and which is regarded by many who knew him best as his greatest accomplishment. In our efforts to practise and improve the healing art we need take no stock of where a man originates but only of what he is. In penning these few lines I cannot but be reminded of the words of the great Scottish poet, Robert Burns, who expressed this idea so vividly when he wrote:

"The rank is but the guinea stamp,
The man's the gowd for a' that."

None the less those of us who know the tradition and reputation of Johann Mikulicz-Radecki can assure Dr. Galewski of our great interest in his communication and of our sympathy for his point of view, especially at this time in the world's history; but I would like to emphasize those other aspects which I have tried to express in these few halting words.—I am, etc.,

Taplow, Bucks. G. GREY TURNER.

Male Toads Croak when Tickled

SIR,—The paper by Drs. J. F. D. Frazer and F. X. Wohlzogen (*Journal*, August 5, p. 330) is of great importance for small laboratories because of the general availability of toads. However, having considerable experience in the use of our local toad (*Bufo arenatus*), I know that anyone trying to perform the test runs into the great difficulty of distinguishing male from female toads. None of the papers on the subject mentions this important point. After consulting a zoologist we now know that only male toads croak when tickled on the throat. A secondary characteristic of male toads is the black thumb on the forelegs. For the tropical climate the toads are preferable not only because of the very high price of *Xenopus* but also because of its poor resistance to temperatures over 85° F. (30° C.).—I am, etc.,

Almirante, Panama. GUSTAV ENGLER.

A Vestigial Tail

SIR,—I was interested to read (*Journal*, October 14, p. 870) the account by Mr. P. J. Blaxland in which reference is made to a similar case which I described in the *Journal* in 1934. It is stated that I suggested that the tail should be left, in the hope that the bearer could subsequently earn his living in a circus. This is incorrect, as the suggestion was offered by one of the relatives, and the advice given to the parents was that "the presence of such an abnormality would affect the child psychically." The parents agreed, and I removed the tail before they changed their minds.—I am, etc.,

London, W.1. R. J. MCNEILL LOVE.

Medical Notes in Parliament

DOCTORS FOR THE FORCES

Man-power, Pay, and Isolation

In the House of Lords on October 18 Lord HADEN-GUEST moved a motion urging greater integration of the National Health Service, the medical services of the Army, Navy, and Air Force, and the medical services of the Colonies. He said that even with the utmost economy and most careful arrangements the country had not enough doctors to do all the work that was necessary. The National Health Service employed over 90% of the available doctors in England and Wales, but the Colonial Medical Service was inadequately supplied with doctors, and the medical branches of the Forces had difficulty in keeping abreast of their requirements. In any sudden emergency partial or complete mobilization could be fully met by calling up doctors who were reservists of the Regular Army, doctors who were in the Territorial Army, and doctors with Class Z liability as having served in the last war. As the result of personal visits which he had paid to commands in this country and overseas he assured the House that the necessary work in the Services was being done despite the difficulties, but it was being done under great strain. Conditions were not fair to the Services at present, and he believed it necessary to bring the civilian and military medical services closer together. The N.H.S. contained about 19,000 general practitioners, about 5,500 consultants, and about 3,500 senior hospital medical officers and senior registrars—a total of 28,000. Doctors in the armed Forces numbered about 2,500, and the number in the Colonial Service was about 1,900.

There was much co-operation between the Services: abroad the sick of all could be admitted to a common hospital. In York a hospital was shared by the Army and the National Health Service, and the latter would accept Service patients in the same way as it accepted anyone else.

Many young doctors now qualified or about to qualify had served in the second world war before their medical studies began, and were therefore no longer liable to conscription. The terms offered for short-service commissions for both men and women were not regarded as attractive at present by either, and the response was poor. In the Colonial Medical Service the situation was also serious, and to secure an inflow of doctors to that Service it had been necessary for the Medical Priority Committee to recommend that doctors who accepted certain Colonial Office posts should be regarded as discharging liability to military service. That arrangement operated in Hong Kong and West Africa. In this country the deficiency in the number of Service doctors could partly be made up by employment of civilian medical practitioners. It had even been found necessary to employ full-time civil surgical and medical consultants in the Services. These men served and dressed as civilians. They received civilian rates of pay which were higher than those of the officers in the unit in which they served, and in some cases higher than that of the Director of Medical Services of the Army formation of which the unit was part. That could not be described as satisfactory, and invalidated any arguments which the D.M.S. might put forward to a junior medical officer in trying to persuade him to take a short-service commission. The situation resulted in officers in Service hospitals being divided into two groups, a top group of regular officers and a lower group of junior officers, with nobody between. The junior group was composed exclusively of National Service doctors. The top group was composed of doctors with regular commissions. This threw an unfair strain on senior officers and ought to be ended as soon as possible. Service pay compared unfavourably with that obtainable in civil life, and Service life cut the man off from his profession, limited his medical experience, and took him abroad. Much the same objections applied to recruitment for the Colonial Medical Service.

Suggested Changes

He suggested that conditions of entry to the medical services of the armed Forces and of the Colonial Medical Service should

be changed and put on an equality with the National Health Service. Every qualified doctor, unless he opted out, should from the time of his qualification and registration be on an equal footing, eligible for the same pension and other rights on the terms and conditions applicable to the National Health Service. He wished to keep the medical services of the Navy, Army, and Air Force separate, as also the Colonial Medical Service, but to make the financial basis the same for all of them, and to allow the young doctor to apply for any of these branches of service but to maintain his pension and other rights, just as he did now if he applied to go to a hospital in another town. Some steps in this direction had been taken by the Ministry of Health. A doctor in the National Health Service who was called up to the Forces could maintain his N.H.S. superannuation by payment of contributions, and a doctor taking a short-service commission in the Forces might do the same. So could a doctor on a short-service commission who took employment in the Colonial Medical Service for six years or less. Such arrangements were not enough to deal with the situation. Unless the pay received by medical officers in the three Services and in the Colonial Medical Service was equal to that received by doctors in the National Health Service, the recruitment required would not be obtained.

At present military service was too often regarded as an interruption in a medical career. Integration of the medical services of the Forces and Colonies with the National Health Service would bring all more closely together. He had been unfavourably impressed at discovering a wide gap in this country between the doctors in the National Health Service and those in the Forces. In one important city which he had recently visited with colleagues of the Medical Priority Committee a leading local practitioner did not know that two Service hospitals existed in it. In another city he and his colleagues visited a hospital which was shared between one of the Services and the regional hospital board. Both parties were enthusiastic about the value of this co-operation, but the existence of the hospital was unknown to some of the leading local civilian medical authorities. In two university towns the Army medical authorities of important areas had only the most distant relations with the medical side of the universities. He suggested a formal link should be created by the Ministry of Health between chief representatives of the medical branches of the Services in the commands, the chief representatives of the National Health Service, and the chief representatives of the medical side of any universities in the areas.

The Specialist Position

Lord Moran said shortage was the fundamental fact. In the Colonial Service 1,500 specialists were necessary, but it was about 200 short. The R.A.M.C. required 455 specialists, but had only 197. It also had 157 who were known as "graded specialists," but these were not specialists at all and would be called junior registrars in the National Health Service, where they would work under supervision. In June, 1949, when reinforcements were needed for the garrison of Hong Kong, three large military hospitals in England had to be closed to provide the necessary specialists.

The remedy was to make conditions in the R.A.M.C. such as would attract specialists in the open market—in other words to pay them more. The Treasury or the Cabinet had sat long over that question. They had recently raised the pay of everyone in the Army except the doctors. That was because the scarcity of consultants in the R.A.M.C. was concealed by men serving as specialists who were not specialists at all. That state of affairs lowered the morale of the R.A.M.C. and lowered the standard of treatment given to men in the Army.

The other remedy was to second for two years to the R.A.M.C. specialists from the National Health Service who had spent five years in a specialty and had senior degrees. The Medical Priority Committee would decide how many men should be so seconded, but it was no use transferring specialists from the National Health Service if there was a shortage in that Service itself. He asked whether there was a shortage of specialists in the National Health Service. The Ministry of Health report which was concerned with the development of consultant services had estimated that 7,000 whole-time specialists were needed. Actually there were in England and Wales 5,200 part-time specialists. That meant that the Service had only 56% of the number aimed at. It was only fair to the Minister of Health to say that the figure of 7,000 was the ultimate aim, but nevertheless a shortage was evident.

Distinction Awards

Lord Moran said he had recently visited the North to ask help in recommendations for his Awards Committee for specialists. When the recommendations came in he was surprised to find the name of only three physicians outside the teaching hospital in that region. The public had been educated to think that surgery was safe only when performed by a surgeon with surgical training. It had not been so educated about medicine. In many parts of England a patient could not get a physician's opinion. He was fobbed off with a doctor who might not be familiar with the weapons which had been placed in physicians' hands in the last 20 years. One of the greatest administrative needs in health matters was that everyone who needed a consultant physician should be able to get one.

If the House accepted his assumption that there was a shortage of specialists in the National Health Service, the whole situation altered. It was little use then in seconding a man from the National Health Service except in an emergency. In an acute shortage in an area it might be sensible to transfer the person from Region A to Region B, but as a long-term policy that was no use at all. The fundamental task of the House that afternoon was to say how the country could get sufficient specialists so that there would be enough for every service.

What did they ask a man to do if they asked him to be a specialist? For five or six years before he qualified he would compete with others, and for five years after qualifying he would compete for registrar posts, and finally for the hospital staff itself. If he left school at 18 and became a specialist at the age of 32—which was the usual age—he would have passed through a course of intensive application, concentration, and will-power spread over 14 years. No other members of the profession were required to spend those years in training. What inducements was Parliament able to give them to make this effort to climb the ladder? In medicine, perhaps more than in other callings, men who had a vocation were not obsessed by material reward, but in these days of penal taxation it was necessary for men to think of their dependants. He said bluntly that the country would not get the specialists required unless it was prepared to give adequate material rewards. He therefore intended to discuss the remuneration of specialists.

The Spens Committee, which had advised the Government on the remuneration of specialists, had begun by inviting Professor Bradford Hill, a statistician, to investigate the income-tax returns of a large number of specialists before the Act had come into force. His report had great influence with the committee. That committee's report on remuneration was a compromise between the merits of seniority and the merits of distinction. Beginning at the age of 32 the specialist, if he devoted all his time to the Service, was paid £1,700 per annum. The specialist was about one-tenth of the whole profession. By gradually increasing increments he rose until at the age of 40 he would receive £2,750 per annum. Thereafter he would receive no rise whatsoever for the next 25 years unless he was chosen for a distinction award. The profession would be one in which a man reached his peak of remuneration at the age of 40 and thereafter received no rise for the rest of his working life. With affairs in that condition they would not get into medicine the men they sought. He thought, therefore, that the awards (which were the other part of the system of remuneration) were of fundamental importance.

Unless the House understood the scope of these awards it was impossible to grasp the problems which were faced to-day. The Government had decided that as there were 5,200 specialists in England and Wales awards should be given to one-third of them, which was roughly 1,700. Of these, 200 should get A awards, 500 B awards, and 1,000 C awards. Those who got the maximum income, which meant they must be whole-time specialists, were a mere fraction of the 200 in the top group, and

that fraction was out of 50,000 doctors. When an award was given to a man it was given only in proportion to the time he devoted to the Service. If half-time were given to the Service, half the award was received. A central committee of 14 acted in a judicial capacity gathering evidence, examining it, and then pronouncing on the awards. The evidence might be provided by the three Royal Colleges and the 14 faculties. That evidence concerned what a man wrote, his contributions to medical meetings, and his technical excellence. The Royal College of Physicians had spent weeks grading more than 3,000 physicians.

Importance of Local Consultation

But it was obvious that many specialists did not write much, were not regular attenders at meetings, and yet were valuable members of the profession. Therefore the central committee required peripheral evidence. That evidence was concerned with how the man pulled his weight, and whether he discharged hospital duties faithfully. It was obtained partly from the regional hospital boards, but that was not sufficient. If it was suggested to Bradford that the regional centre in Leeds should judge for Bradford, they would have a riot. It was necessary to get the pronouncements by the man's own colleagues. The central committee had held 58 meetings all over the kingdom, with an average attendance of between 30 and 40. These meetings had elected committees of three to help in grading specialists who were not attached to teaching hospitals but worked outside great university centres. In spite of all this care the committee felt the danger of error and constantly took, as it were, insurances against error. A London surgeon, for example, might easily have eight different gradings. The committee liked to wait for the time when all those gradings pointed in one direction. It then knew that it was doing what the judgment of the profession would consider right.

Again, the committee knew the number of specialists in the region and so could work out what would be the expectation of that region in awards if they were given by arithmetic. If it then found that one region had done badly, the committee would say there was a call to go over the facts again from the beginning. The committee went through the same process with each specialty in each region, and if one specialty had done badly it went through the evidence again. In that way it tried to establish a degree of exactitude in the awards. He felt that these awards were important in retaining the efficiency of the whole Service. If they were abolished, it would adversely affect the quality of men seeking admission to medical schools, because medicine, like other professions, must appeal competitively to the man of promise. As a man who had been dean at a medical school for 25 years, he said that but for these awards medicine could not compete successfully with other professions for the man of promise. He reminded the House that as far back as they could remember almost every addition to medical knowledge had come from specialists attached to hospitals. If the awards were abolished, men in medical schools would be discouraged from specialism, and there would be scarcity of specialists and a fall in hospital standards.

He did not believe any Government would scrap the award system without first giving it a trial. If the financial circumstances of the country made it necessary to have a percentage reduction in the salaries of every profession, medicine would gladly bear its share, but to take a fraction of a single profession and confiscate a considerable proportion of the income of that fraction was not in accordance with justice.

Before the Health Service Act there had been many grades of hospitals. One of the first purposes of the Service was that there should be one grade of hospital. Up-grading of backward hospitals could be done only by strengthening the staffs, and the only way to do that was by decentralization of specialists. These had tended in the past to congregate in great centres of population, and the awards would help decentralization by making a man less dependent on private practice. He had spent the last three months going through England and Wales talking to specialists, and could say that these, with a few noisy exceptions, not only favoured these awards but would be shocked if they were withdrawn. The Ministry of Health saw clearly that the specialist in the past had been accustomed to the stimulus of a competitive profession, but that he felt a weakening of that impulse, and that another incentive was necessary.

Opposition to the awards did not come from the desire for economy. Such hostility as there was came largely from an old feud. In 1918 recommendations of a Royal Commission had been implemented, and professors of medicine and surgery were for the first time paid salaries in England. These salaries were in excess of those of professors of non-medical faculties. For more than 30 years successive governments had accepted this. Unfortunately when the awards were introduced vice-chancellors of universities, urged on by non-medical faculties, had renewed the attack, although only a mere handful of specialists was concerned—a few professors of medicine and surgery, and a few pathologists, and the like. Medicine had seemed to him two years ago like a great tree uprooted in a storm. If someone now wished once more to tear up that tree by its roots, then he, who had no politics, would despair of that folly.

Medical Services and War

Lord Boyd-Orr said he proposed to speak on the integration of the medical service as an essential part for the preparation of war. Almost until the second world war deaths, injuries, and diseases caused by war so differed from those that befell the civil population that medical officers had to receive a special training to deal with them. If war came now the whole nation would have to prepare not only to face atomic bombs but also biological weapons, which according to Dr. Chisholm, who had been a major-general in the Canadian Army in the first world war and in charge of research in the recent war, would kill more people than the atomic bomb. Civilians and soldiers would suffer the same injuries or diseases, and there was therefore every reason to co-ordinate all branches of the medical services. Co-ordination of home industries, supply and production of food, of hospitals, and of the treatment of diseases were all interlocked. He suggested an even closer integration of the medical services than that proposed by Lord Haden-Guest.

Links With the Colonies

Lord Amulree emphasized the advantage of joining the medical services in the Colonies with those in Great Britain. He asserted that the general standard of medicine in this country was probably higher than in any other country in the world, and it was desirable to spread among the Colonies the same high standard. He would like to see many more exchange visits by doctors from Great Britain to the Colonies. He knew what a great encouragement it was to a doctor in some out-of-the-way Colony if someone came out there for six months or a year, someone of considerable fame in his own specialized work. It was also of great value to medical men who worked in these Colonies if they could come back to Britain at more regular intervals than they did now and could obtain some kind of employment, not merely a refresher course. In 1947, when he went to China on a parliamentary visit, he met a Chinese doctor aged about 50 who had been trained in Great Britain and had done extremely well as a surgeon. Since returning to China he had never been back to Britain and felt that he was losing his grip and was being dragged down into something he certainly had not been. Various doctors of the British community who had been in China for a long time said that for the first ten or fifteen years they had got on quite well, but thereafter, because they had no one to discuss things with and could gather no more experience, they felt they were falling back. Lord Amulree said he would like to see more patients brought from the Colonies to Britain for specialized and difficult treatment, particularly of cancer. It was extremely costly to provide *x*-ray machines and radium installations all over the world, and moreover these needed to be used by people of great skill and experience. He would like to see more people brought from the Mediterranean Colonies and African Colonies, not only European members of the populations but natives also, for treatment of these diseases. If one or two were persuaded to come and return home successfully treated that might be the start of a large temporary immigration of the sort he suggested.

Lord Marley said that financial payment for both home and Colonial work must finally rest on the productive capacity of

workers in the United Kingdom. At present on the average one million workers were away from industry all the time through sickness, representing an annual loss of production of something like £400m. Therefore it was vital that the National Health Service should be at least on a par with the overseas service. Yet general practitioners complained that they were overworked and that their incomes were inadequate, and there were suggestions that they might withdraw from the National Health Service. If that happened it would have a disastrous effect on the work of eliminating sickness among the working population. There must be not fewer than 2,500,000 in this country requiring medical attention. It behoved Parliament to make certain that all the medical services were adequately remunerated and that equally attractive conditions existed in each. Lord Marley went on to draw attention to the condition of radiographers, who were deprived of what was called the London weighting for those employed in London. These people had high qualifications and were engaged in a dangerous occupation. In other not dissimilar services, such as that of electroencephalographer, the London weighting payment was available. Such things were likely to discourage the best medical students and the best of other scientific workers from joining in the National Health Service, the Colonial Service, or the fighting Services.

Secondment and Redistribution

Lord Webb-Johnson recalled that he had spoken on the same subject in December, 1948, when the Government representative had promised to see that his remarks were conveyed to the Minister of Defence. He had spoken again last April, when he had pointed out that there was a 37% deficiency in the R.A.M.C., and Lord Alexander had said that he would have every opportunity of casting stones if nothing had been done in the matter by the next time it was debated. Lord Webb-Johnson felt that the peers should support a demand that terms and conditions of service for the medical branches of the Forces should be dealt with immediately. There was no excuse for further delay. There was no basis for an integration of the various medical services until the rates of pay were settled. He thought that secondment not only from N.H.S. to the Forces and Colonial Service but also in the other direction would be of great value. Two distinguished officers of the R.A.M.C. had been seconded, one to the Iraq Government and the other to the Saudi-Arabian Government, and they would return to the seniority in pay and rank which they would have reached if they had stayed with their corps the whole time. Within the last fortnight the Colonial Office had issued a document arranging for superannuation pensions to be carried on if a medical officer left the National Health Service and within twelve months entered the Colonial Medical Service.

The Marquess of Salisbury recalled that he had been for some time during the war chairman of a committee of Ministers set up to allocate the supply of doctors between the armed Services and the civil population. As a result he formed the opinion that there must be some permanent scheme to operate in peace and war if the needs of military and civilians and also of the Colonial Empire were to be met. When war broke out in 1939 doctors with complete patriotism agreed that some should be diverted to the assistance of the armed Forces. By the later part of the war the civilian population was served by only a residue of elderly doctors and a few who had not been passed fit for military service. The Government had then had to face the necessity of withdrawing some doctors from the armed Services. With demobilization the balance swung back, and the position at the moment was comparable to that in 1939. Such violent fluctuations were not satisfactory in peace or in war. It might be, as Lord Moran had said, that there were not enough doctors to go round, but that did not seem to be a reason for failing to strike the best practicable balance. It seemed to be vital for the Government and the medical profession to devise some scheme to ensure a fair flow of medical practitioners to where they were needed. What was required was closer integration between the medical services by way of secondment from one to the other. He did not know whether it was practicable to assimilate the rates of pay in the three branches of medical work, but they ought to be brought as near as possible to each other. That applied equally to the specialist, about whom Lord Moran had spoken. Let the Government if necessary set up a Cabinet committee and let it make one Minister responsible for the problem.

Government Reply

Lord Shepherd replied for the Government. He said the work of the medical priority committee had considerably helped to ease the difficulty in the staffing of the branches of the medical services and to alleviate the problems of the Colonial Medical Service. In the Forces there was a shortage of 400 specialists and of 100 general-duty doctors. In the Colonial Service the shortage was 200. These figures need not cause alarm provided that the Government of the day and the medical profession were concerned about the situation. He was sure that with better organization and conditions Parliament would be able to change the deficit into a sufficiency.

In 1930 the number of registered doctors was 54,537, of whom 9,000 resided abroad. In the present year the number on the *Register* was 77,730 and the number resident abroad was 12,000. Was this an increase upon which they could depend for feeding the Forces with their extra requirements? They had to think of the large number of women now registered as doctors. Lord Haden-Guest pointed out that of these women 50% did not practise. The second thing to remember was age. Only younger members of the profession could be attracted into the Services. National Health Service demands were so large that they must have reduced the availability of doctors for the Services. He believed they not only had to think of transferring men and women into the Forces or into the Colonial Empire but of how they could recruit more doctors, both men and women, into the profession. In 1946 of men who became qualified only 44% were prima facie available for military service. The rest had completed their military service before they qualified. In 1947 the proportion was 53%, in 1948 54%, and in 1949 58%. The Minister of Labour had compiled figures for the period 1950–4 indicating that the proportion of men available would again drop. In those years, of 9,653 men who expected to qualify no more than 4,900 would be available for service, a ratio of 50%. Of these probably 20% would be considered to be militarily unfit. It therefore seemed that the intake under conscription might not be sufficiently large to cover the deficiency in the Forces.

Since 1939, 20,000 doctors had done military service and had gone into private practice or hospital service. They were unlikely to be disturbed, although in times of emergency they would answer the call. Some of these men were still on the reserve, but their period of reserve service would soon be finished. Nobody had suggested that for the rest of the medical population there should be compulsion, although he was not clear what Lord Moran and Lord Webb-Johnson had meant when they spoke of seconded people for service. He gathered that Lord Webb-Johnson had not advocated compulsion.

Inducements for Specialists

Lord Moran had suggested that greater inducements should be offered to specialists. At this moment a number of medical men, at the request of Mr. Bevan, were inquiring into the circumstances of medical students. There seemed to be a preponderance of men and women who desired to be trained as specialists and not as ordinary medical practitioners. It seemed therefore that the inducements already given were sufficient. The Minister of Health wanted to use his influence and that of hospital and university authorities to persuade some of these would-be specialists to reconsider their position and to take early service in the Army as general medical men. Men could now be transferred, or might transfer, from the ordinary health services into the other Services at home or abroad, and could arrange with the authorities to continue their pension rights without losing seniority. Hospital authorities had been advised, or were about to be advised, that it would be good if part of their own medical staffs had experience of the Colonies or of the Forces.

Future Co-ordination

The Government was satisfied that it had not gone far enough and desired to meet the case put forward by Lord Haden-Guest. An interdepartmental committee was considering co-ordination of medical services within the Forces and within the Health Service. He hoped that something good would result from this inquiry.

Lord SWINTON said it was desirable that, where there were Service Ministers and civil Ministers on an inquiry, each of them with a Department, there should be an independent Minister in the chair. He thought a similar arrangement would be wise if the committee consisted of senior officials.

Lord SHEPHERD replied that the interdepartmental committee did consist of senior officials but that he would see that the suggestion made by Lord Swinton was brought forward. Continuing, Lord Shepherd said the Government had recently considered the position of the Medical Priority Committee and of the Committee of Reference which had similar functions in relation to hospitals in the London area. A meeting was to take place that week between the Government and those concerned to consider the future of these bodies. If it was possible to get friendly co-operation between the bodies, or to integrate them, the advice given to the Government would be more concentrated.

Integration with the Services had the blessing of the Government, which would see it through. Dealing with payment for services in the Forces and in the Colonial Service, Lord Shepherd said it was now realized that there must be restrained movement both of wages and of salaries, and the utmost consideration would be given to the claim of medical men in the Forces. Medical men in the Forces ought not to be worse off than medical men in civil life or than men employed on general military duty in the Forces. He was unable at present, however, to make an announcement. That announcement should be made either by the Chancellor of the Exchequer or by the Ministers concerned. The subject had been pressed by the Ministries upon the Treasury. It was not too much to hope that this would be the last time the House of Lords would be bothered about it.

Lord HADEN-GUEST hoped that the last words spoken by Lord Shepherd would be duly implemented in a suitable statement. He then withdrew his motion.

Invalid Port

Mr. J. A. BOYD-CARPENTER moved on October 17 that the Labelling of Food Order, 1950, be annulled. This provided, *inter alia*, that no one should have in his possession for sale any liquor the label on which was

> by any name or words calculated to indicate, either directly or by ambiguity, omission, or inference, that the liquor had properties which made it beneficial to invalids, or had tonic, restorative, or medicinal properties unless the liquor contained a substance or substances other than alcohol added in such quantity as to confer such properties.

Mr. Boyd-Carpenter understood that this rendered illegal the use of the expression "invalid port."

Mr. F. T. WILLEY, Parliamentary Secretary to the Ministry of Food, said there was no difference in substance between invalid port and other port. Medical advice had always been that such misleading descriptions should be prohibited.

Dr. CHARLES HILL said nothing in the Order precluded the most fantastic claims which an advertising genius could make for fluids containing alcohol, on the assumption that these fluids did not purport to be foods. A great deal of the publicity which was intended to suggest a nutritional quality in alcoholic beverages was based on a fantastic conception of what such food could do to sustain the human frame. The fact that alcoholic drinks did not contain building or other nutritional elements need not necessarily condemn them. He was not overlooking the effect which such properties had on the higher centres of energy and on human worries and sense of fatigue. If the purpose of the Order was to prevent the making of false claims it would be desirable to address attention to the falseness of the claims which were made for the food value and building value of such liquids as had on other grounds much to commend them to many in the House. He would rather see these excellent fluids properly described, without the pretence that they were of particular value to expectant and nursing mothers, or that they had any nutritional value worth considering.

After further discussion, Mr. Boyd-Carpenter's motion was rejected.

Universities and Colleges

UNIVERSITY OF CAMBRIDGE

The following degrees were conferred on October 14:

M.A.—D. M. T. Gairdner, D.M.

M.D.—A. Lyell, Mary Farquharson.

M.B., B.CHIR.—*J. F. Hort, *J. F. Lees, *G. Holden, *J. D. Jackson, R. P. Ross.

* By proxy.

UNIVERSITY OF EDINBURGH

Professor R. A. Peters, F.R.S., Whitley Professor of Biochemistry in the University of Oxford, will deliver the Cameron Prize Lecture on "Applications of Chemical Defence Research in Medicine" in the Anatomy Lecture Theatre, University New Buildings, Teviot Place, Edinburgh, on Monday, November 6, at 5 p.m. Students and graduates are invited to attend the lecture.

UNIVERSITY OF LONDON

The following candidates have been approved at the examinations indicated:

ACADEMIC POSTGRADUATE DIPLOMA IN CLINICAL PATHOLOGY.—D. Baidya, I. A. Blackmore, V. St. E. D'Abrera, Phyllis Dagnall, J. L. Holme, A. Husain, O. G. Jones, Endre Kertész, F. Kurrein, M. Millard, G. P. Mohanty, H. Prasad, W. D. Ratnavale, Rosemary J. S. Sichel, M. L. Sur, A. Tay, L. Vogel.

EXTERNAL DIPLOMA IN CLINICAL PATHOLOGY.—G. T. Barnes, K. S. Daber, N. P. Jain, J. K. F. Mason, J. B Neal.

UNIVERSITY OF WALES

WELSH NATIONAL SCHOOL OF MEDICINE

Professor F. R. G. Heaf will deliver an inaugural address on "Infection and Disease, with Special Reference to Tuberculosis" in the Reardon Smith Lecture Theatre, Park Place, Cardiff, on Thursday, November 9, at 8 p.m.

UNIVERSITY OF LEEDS

At a meeting of the Council of the University held on October 18 the title of Emeritus Professor was conferred upon Professor M. J. Stewart, LL.D., M.B., Ch.B., F.R.C.P., on the occasion of his retirement from the Chair of Pathology. The Council expressed the wish to be joined in the Senate's resolution of warm appreciation of his work. Professor Stewart was a member of the Senate for thirty-two years. He served also for long periods in many posts of administrative responsibility in the School of Medicine, and as Pro-Vice-Chancellor.

Other appointments were made as follows: R. E. Coupland, M.B., Ch.B., as Lecturer in Anatomy (from October 1); G. Watkinson, M.D., M.R.C.P., as Lecturer in Medicine (from October 1); J. A. L. Vaughan-Jones, M.B., Ch.B., J.P., as part-time Lecturer in Public Health for the session 1950–1.

The Council recorded its congratulations to C. W. Dixon, M.D., D.L.O., D.C.H., D.P.H., Lecturer and Chief Assistant in the Department of Preventive Medicine and Public Health, on the award of a Leverhulme Research Grant for 1950–1 to enable him to carry out research in the epidemiology of smallpox and control of variola minor.

UNIVERSITY OF SHEFFIELD

Dr. Lorna H. Heslop has been appointed assistant medical officer to the Student Health Service of the University.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

The Frederick Hewitt Lecture will be delivered by Dr. George Edwards before the Faculty of Anaesthetists of the Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C., on Wednesday, November 1, at 5 p.m. His subject is, "Frederick William Hewitt."

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

On October 18 Dr. Leonard Abrahamson was elected President of the College and Dr. G. T. O'Brien Vice-President.

Dr. R. S. F. Hennessey was admitted, *in absentia*, to the Fellowship of the College on October 6.

No. 40

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended October 7.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1950 (a)	(b)	(c)	(d)	(e)	1949 (Corresponding Week) (a)	(b)	(c)	(d)	(e)
Meningococcal infection	30	3	13		2	37	4	16	2	1
Deaths		—	2				—	—		
Diphtheria	40	6	11	5	6	84	11	22	4	5
Deaths	—	—	—	—	1	—	—	—	—	—
Dysentery	187	14	149	2	1	290	16	78	—	2
Deaths		—			—				—	—
Encephalitis, acute	4	—	—		—	1	—	—	—	—
Deaths		—		—			—			
Erysipelas			19	12	2			17	8	3
Deaths							—			
Infective enteritis or diarrhoea under 2 years				19	17				107	
Deaths	8		1	4	—	36	2	7	9	5
Measles*	3,914	289	197	87	66	926	28	43	75	35
Deaths†		—	—	—	—			—	—	—
Ophthalmia neonatorum	32	2	5		—	31	4	3	—	1
Deaths										
Paratyphoid fever	11	2	1 (B)		1	18	—	1 (A) 6 (B)	2 (B)	—
Deaths	—		—		—	—	—	—	—	—
Pneumonia, influenzal	351	10	3		6	312	15	1	—	6
Deaths (from influenza)‡	8	—	—	1	—	7	—	—	—	—
Pneumonia, primary			134	¶				133	21	
Deaths	131	18		4	12	137	18		7	5
Poliomyelitis, acute	353	20	49	6	4	374	53	6	3	2
Deaths§	25	1		1		17	—			
Puerperal fever			6				—	2		
Deaths										
Puerperal pyrexia‖	74	3	10	2	2	114	19	6	1	1
Deaths							—			
Relapsing fever	—	—			—	—	—			—
Deaths										
Scarlet fever	1,064	90	162	70	61	1,624	114	202	99	163
Deaths†		—	—	—	—			—	—	—
Smallpox	—	—	—		—	—	—	—	—	—
Deaths					—				—	—
Typhoid fever	10	2	2	—	1	18	2	3	1	1
Deaths	1	—	—		—	—	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths					—				—	—
Whooping-cough	2,445	255	222	53	21	908	31	47	26	41
Deaths	4	1	—	—	—	5	—	—	—	—
Deaths (0–1 year)	203	22	32	10	12	293	23	39	22	16
Deaths (excluding stillbirths)	4,529	681	546	145	105	4,124	567	529	147	112
Annual death rate (per 1,000 persons living)			11·0					10·6	9·1	
Live births	7,546	1217	930	368	259	7,993	1293	976	394	235
Annual rate per 1,000 persons living			18·7					19·6	24·4	
Stillbirths	147	15	20			177	13	28		
Rate per 1,000 total births (including stillborn)			21					28		

* Measles is not notifiable in Scotland, and the returns are therefore an approximation only.

† Deaths from measles and scarlet fever for England and Wales, London (administrative county), will no longer be published.

‡ Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

§ The number of deaths from poliomyelitis and polio-encephalitis for England and Wales London (administrative county), are combined.

‖ Includes puerperal fever for England and Wales and Eire.

¶ Primary pneumonia no longer notifiable in Eire.

EPIDEMIOLOGICAL NOTES

Poliomyelitis

The notifications of poliomyelitis in the week ending October 14 were: paralytic, 223 (241); non-paralytic, 85 (112); total, 308 (353). The figures for the previous week are in parentheses. Those for the corresponding week in 1947 and 1949 were 364 and 463.

Total uncorrected notifications for 1950 up to and including the week under review are 7,012. The corresponding figures for 1947, 1948, and 1949 were 7,454, 1,825, and 4,478 respectively.

The only county area in which there was any considerable increase was Hertford, with 7 cases more than in the preceding week. Comparatively large decreases occurred in Devon (8), Gloucester (7), Stafford (16), with smaller decreases in many other counties. Total notifications for the week were fewer than in the preceding week by the following: paralytic, 18; non-paralytic, 27; total, 45.

Discussion of Table

In *England and Wales* increases were recorded in the number of notifications of measles 951, scarlet fever 127, acute pneumonia 70, acute poliomyelitis 22, and decreases were reported for whooping-cough 171 and diphtheria 10.

The largest rises in the incidence of measles were Yorkshire West Riding 147, Lancashire 92, Gloucestershire 86, London 72, and Middlesex 69. The only rise of any size in the local trends of scarlet fever was 43 in London. The chief feature of the returns for diphtheria was a decrease of 5 in Durham. The largest variations in the trends of whooping-cough were decreases in Yorkshire West Riding 70, Lancashire 46, and a rise of 39 in Middlesex.

The largest centres of dysentery were Lancashire 59 (Manchester C.B. 20, Oldham C.B. 10); Yorkshire West Riding 25 (Batley M.B. 13); Leicestershire 23 (Leicester C.B. 22); London 14 (Paddington 5); Surrey 14 (Surbiton M.B. 10); Durham 12. Two large outbreaks of food-poisoning were reported from Yorkshire West Riding—Wortley U.D. 220 and Bradford C.B. 58.

The largest returns of acute poliomyelitis were Lancashire 32 (Manchester C.B. 13, Liverpool C.B. 5); Gloucestershire 31 (Bristol C.B. 22); Yorkshire West Riding 29 (Sheffield C.B. 6); Staffordshire 22; London 20; Devonshire 19 (Newton Abbot R.D. 9); Kent 18 (Orpington U.D. 10); Warwickshire 16 (Birmingham C.B. 12); Durham 13; Surrey 12 (Croydon C.B. 4); Middlesex 10; Glamorganshire 10.

In *Scotland* increases were recorded in the number of notifications of measles 51, dysentery 22, and whooping-cough 21, while the only fall of any size was 47 for scarlet fever. The largest returns of dysentery were those of the cities of Glasgow 70, Edinburgh 21. Dumfries 17, Stirling county 12, and Lanark county 11. The notifications of acute poliomyelitis were 7 fewer than in the preceding week; the chief centres of infection were Glasgow 9, Angus county 8, Dundee 6, Motherwell and Wishaw 4.

In *Eire* increases in the number of notifications of measles 44 and scarlet fever 30 were recorded. The rise in the incidence of scarlet fever was mainly contributed by Dublin C.B., where a rise of 18 was recorded. The increase in measles was due to outbreaks in Dublin, Balrothery R.D. 19, Meath, Painestown R.D. 12, and Tipperary, Nenagh R.D. 10.

In *Northern Ireland* a rise of 23 was reported in the number of notifications of measles. The largest increase in the incidence of measles was 22 in Antrim county. Only 4 cases of acute poliomyelitis were notified, a decrease of 6 from the preceding week.

Week Ending October 14

The notifications of infectious diseases in England and Wales during the week included scarlet fever 1,193, whooping-cough 2,461, diphtheria 40, measles 5,009, acute pneumonia 382, acute poliomyelitis 308, dysentery 180, paratyphoid fever 8, and typhoid fever 7.

Medical News

Presentation to Dr. E. A. Gregg

Dr. E. A. Gregg, Chairman of Council of the B.M.A., was on October 24 presented by the London Local Medical Committee with a wallet containing a cheque, in recognition of his many years of devoted service in the interests of the general practitioners of London. Dr. Gregg joined the London Local Medical and Panel Committee in 1919. He was chairman of it from 1936 to 1949, and among his other duties represented the committee on the Insurance Acts Committee, of which he was also chairman. After the presentation Dr. Gregg, expressing his gratitude for the gift, emphasized the importance of the work of local medical committees.

Harveian Dinner

A Commemorative Feast, which William Harvey ordained should take place yearly on St. Luke's Day, was held on October 18 at the Royal College of Physicians of London. The Fellows of the College entertained the following guests: Lord Addison, Professor Lillian Penson, Sir Edward Peacock, Sir Wilson Jameson, Sir Cecil Wakeley, P.R.C.S., Sir Henry Hake, Sir Leonard Parsons, F.R.S., Professor Hilda Lloyd, P.R.C.O.G., Professor B. W. Windeyer, and Mr. Geoffrey Keynes. The toast of "The Immortal Memory of William Harvey" was proposed by the President and replied to by Sir Leonard Parsons, the Harveian Orator.

Colney Hatch Centenary

Friern Hospital, formerly known as Colney Hatch Asylum, celebrated its centenary on October 27. In 1847 a committee was appointed by the Middlesex Justices of the Peace to find a suitable site for a building to accommodate 1,000 patients. In May, 1849, the Prince Consort laid the foundation stone, and the Queen subscribed £100 to open the "Victoria Fund" to assist those discharged as cured. This fund was merged later with the Queen Adelaide Fund. When the building was ready for occupation in October, 1850, it was described as being "unrivalled as a lunatic asylum, unique in size, elevation, and accommodation in this country or perhaps any other." The cost amounted to £138,000, to which was added the cost of equipment, a further £110,000. At that time the treatment of mental troubles was primitive. The first thing that happened when a patient was brought to Colney Hatch was the removal of strait-jackets and other restraints. The only "seclusion" practised was the confinement for their own safety of patients who became violent: and even the padded cells had half-doors to reduce actual seclusion to a minimum. By the third year there were 1,250 patients at Colney Hatch. During 1852, 17 patients escaped, all of whom were traced and brought back. Within five years it had become necessary to raise the accommodation to over 2,000. Later, additional wards were erected apart from the main building, and when these were destroyed in 1903 by a fire, in which 51 women lost their lives, they were replaced by brick villas. These in turn suffered very severely from enemy action in the second world war. More recently, new admission wards and a nurses' home have been erected. To-day there is accommodation for some 2,500 patients and 800 staff.

London Hospital Dinner

The London Hospital Old Students' Dinner was held on October 19 at the Trocadero, with Sir James Walton in the chair. The guests included the regius professors of medicine of the Universities of Oxford and Cambridge, the Directors-General of the Royal Navy and the Army Medical Services, Sir John Charles, Sir Gordon Covell, and Dr. F. M. R. Walshe, who earlier in the day had delivered the Schorstein Lecture at the London Hospital. In proposing the toast of the London Hospital, the chairman referred to the guests, the activities of the year, and the changes that had occurred in medicine in his time, concluding with wise counsel for the retired and those near the retiring age. Sir Henry Tidy proposed the health of the chairman.

An Early Radiologist

A delightful address was given from the chair of the British Institute of Radiology by Dr. R. Fawcitt, its new president, on October 19. It was a description of the life of a country doctor in Cumberland who combined with general practice the work of a radiologist. Dr. Fawcitt inherited his practice from his father, who carried on his work in the fells in a gig, on a bicycle, or on foot, and only in the last few months of his life—he died in 1913—would look at a motor-car. Most of the early radiologists, said Dr. Fawcitt, started life as general practitioners. His own interest in the subject dated from 1910. Many of them had little training in radiology at all. In the early days some of these practitioners got the D.M.R.E. without any examination. It was sometimes said that they came in by the back door. But it was not the back door nor even the side door by which they entered radiology, it was the front door, because their best equipment was a general knowledge of medicine and surgery, which made them consultants in the truest sense of the word when they had acquired a reputation in the specialty of their choice. The country doctor, said Dr. Fawcitt, was perhaps less likely than others to forget that every patient was an individual. He had sometimes been told in his radiological department that a "chest" was coming at ten o'clock or an "arm" at ten-thirty, and he always inquired whether the chest was coming by itself or the arm did not belong to somebody. Those who chose radiology, he said, had chosen the most exacting specialty in the profession. He spoke of the need for the country doctor to keep himself up to date. "When the doctor ceases to read journals and books of reference something is wrong; either he is hopelessly overworked or he is a sick man. It is time for him to slow down or change his occupation."

Guide to London Hospitals

The King Edward's Hospital Fund for London has prepared an excellent map showing the hospitals and convalescent homes in the Metropolitan Police District. It is on a large scale (1 in. to the mile), and marks the hospitals by different symbols to show whether they are teaching or non-teaching hospitals, what cases they specialize in, and in which hospital board area they are situated. Clearly set out cross-indexes make it easy to find any hospital on the map. The map and indexes, which are bound together, are obtainable for 15s., post free, from the King Edward's Hospital Fund, 10, Old Jewry, London, E.C.2.

Occupational Diseases

The Ministry of National Insurance has produced a booklet, *Notes on the Diagnosis of Occupational Diseases* (H.M.S.O., 1s. 6d.), for the guidance of medical practitioners who are asked by the Ministry to examine and report on claimants for benefits under the Industrial Injuries Acts for prescribed diseases. The booklet gives guidance on the diagnosis of the commoner diseases, symptoms of poisoning, and other disorders met with in industry.

Gift to R.S.M. for Library

At the first meeting, on October 17, of the council of the Royal Society of Medicine for the session 1950–1, with Lord Webb-Johnson, president, in the chair, Sir Henry Dale, O.M., F.R.S., immediate past president of the Society and chairman of the trustees of the Wellcome Foundation, submitted an offer of £80,000 by the Foundation to the Royal Society of Medicine for the purpose of establishing within the Society a medical research library bearing the name of Wellcome which shall be effectively part of the library of the Society. The gift, with the conditions attached, was accepted with enthusiasm and gratitude, and the following resolution was passed:

The council of the Royal Society of Medicine wish to express their deep gratitude to the Wellcome Trustees for their offer of a gift of £80,000 for the purpose of adding to the Society's house an additional library to be known as the Wellcome Library. The council are gratified and proud to add the distinguished name of Sir Henry Wellcome to those memorialized in the Society's house. The council accept the gift, with all the conditions attached, with great relief as well as gratitude, for the need of this extension of their resources has been clear to them for some years and is now a matter of great urgency.

Postgraduate Travelling Fellowships

The British Postgraduate Medical Federation (University of London) is offering a limited number of postgraduate travelling fellowships, tenable for one year, to registered medical practitioners training as specialists in one of the preclinical or clinical branches of medicine or surgery at one of the medical schools or teaching hospitals and postgraduate institutes of the University of London. Further information about these Fellowships will be found in the advertisement columns.

Gift to Ophthalmological Laboratory

The National Council to Combat Blindness, an American charitable organization whose purpose is to finance and stimulate ophthalmological research, has presented a Beckman spectrophotometer to the Nuffield Laboratory of Ophthalmology at Oxford.

"Journal of Neuropathology and Experimental Neurology"

Dr. Joseph H. Globus, 960, Park Avenue, New York, 28, N.Y., has been appointed chief editor in place of Dr. George B. Hassin, who has resigned. Dr. Armando Feraro and Dr. Arthur Weil have been appointed associate and assistant editors respectively, and it is intended to widen the advisory board by including representatives of more research centres, both in the U.S.A. and abroad.

COMING EVENTS

Bradshaw Lecture

The Bradshaw Lecture will be delivered by Dr. E. R. Cullinan, F.R.C.P., before the Royal College of Physicians of London (Pall Mall East, London, S.W.) on Thursday, November 16, at 5 p.m. His subject is "The Clinical Interpretation of Jaundice."

Leeuwenhoek Lecture

Sir Paul Fildes, F.R.S., will deliver the Leeuwenhoek Lecture before the Royal Society (Burlington House, Piccadilly, London, W.) on Thursday, November 9, at 4.30 p.m. His subject is "The Development of Microbiology."

Empire Rheumatism Council

The Empire Rheumatism Council has arranged an autumn week-end postgraduate course to be held at the Apothecaries' Hall, Blackfriars Lane, Queen Victoria Street, London, E.C., on Friday, Saturday, and Sunday, November 17, 18, and 19, with the following programme: November 17, 4.30 p.m., Dr. W. S. C. Copeman, "Fibrositis"; 5.30 p.m., Dr. Oswald Savage, "Cortisone and A.C.T.H. in the Rheumatic Diseases." November 18, 10 a.m., Dr. E. G. L. Bywaters, "Juvenile Rheumatism"; 11.15 a.m., Dr. G. D. Kersley, "Gout"; 2 p.m., Dr. H. J. Gibson, "Pathology of the Rheumatic Diseases"; 3 p.m., Dr. H. F. West, "Rheumatoid Arthritis"; 4.30 p.m., Dr. F. Dudley Hart, "Ankylosing Spondylitis." November 19, 10 a.m., Dr. H. A. Burt, "The Aims of Physical Medicine in the Treatment of Rheumatism"; 11.15 a.m., Mr. W. D. Coltart, "Orthopaedic Aspects of the Rheumatic Diseases." The fee for the course is £2 2s., and entries (limited to 100) must reach the general secretary of the council, Tavistock House North, Tavistock Square, London, W.C.1, at least one week before the course opens.

Kettle Memorial Lecture

Professor L. P. Garrod will deliver the Kettle Memorial Lecture on "The Reactions of Bacteria to Chemotherapeutic Agents" in the Anatomy Lecture Theatre, St. Bartholomew's Hospital Medical College, Charterhouse Square, London, E.C., on Wednesday, November 22, at 5 p.m. Medical practitioners and medical undergraduates are invited to attend the lecture.

Leeds School of Medicine

The 60th annual dinner of past and present men students of the Leeds School of Medicine will be held at the Great Northern Hotel, Leeds, on Friday, November 24, at 7 for 7.30 p.m. All graduates of the school will receive official notification of the dinner, with information regarding tickets, at the beginning of November.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday

●Institute of Neurology, National Hospital, Queen Square, London, W.C.—October 30, 5 p.m., *"Pathological Classification of Cerebral Tumours in Children,"* by Dr. M. Bodian.

Institute of Ophthalmology (University of London), Judd Street, London, W.C.—October 30, 5.30 p.m., *"Chiasmal Arachnoiditis,"* by Mr. A. J. B. Goldsmith.

●Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C.—October 30, 3.45 p.m., *"Tissue Spaces and Synovial Sheaths of the Hand,"* by Professor John Kirk.

Tuesday

British Postgraduate Medical Federation.—At London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C., October 31, 5.30 p.m., *"The Nutritional Requirements of Bacteria,"* by Sir Paul Fildes, Sc.D., F.R.S.

●Institute of Dermatology, Lisle Street, Leicester Square, London, W.C.—October 31, 5 p.m., *"Abnormalities of the Cutaneous Circulation in the Lower Limb,"* by Mr. A. K. Monro.

Institute of Urology (University of London).—At St. Paul's Hospital, Henrietta Street, London, W.C.—October 31, 5 p.m., *"Aetiology, Pathology, and Symptoms of Benign Enlargement of the Prostate,"* by Mr. H. K. Vernon.

●Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C.—October 31, 3.45 p.m., *"Kidneys and Bladder,"* by Professor T. Nicol.

Royal Eye Hospital, St. George's Circus, Southwark, London, S.E.—October 31, 4 p.m., *"Contact Lenses,"* by Mr. C. G. Kay Sharp; 5 p.m., *"Genetics in Ophthalmology,"* by Professor Arnold Sorsby.

University College, Gower Street, London, W.C.—October 31, 5.15 p.m., *"Some Recent Advances in the Physiology of Vision,"* by Professor Hamilton Hartridge, F.R.S.

Wednesday

Edinburgh Clinical Club.—At Industrial Rehabilitation Unit (West Granton Road), Edinburgh, November 1, 3.30 p.m., clinical meeting by Dr. Hugh Miller.

Institute of Ophthalmology (University of London), Judd Street, London, W.C.—November 1, 5.30 p.m., *"Radiotherapy and Diseases of the Cornea,"* by Dr. M. Lederman.

Institute of Urology (University of London).—At St. Paul's Hospital, Henrietta Street, London, W.C.—November 1, (1) 3.30 p.m., demonstration of endoscopic instruments by Mr. A. R. C. Higham; (2) 5 p.m., *"A Survey of the Different Methods of Treatment of Benign Enlargement of the Prostate,"* by Mr. R. Ogier Ward.

●Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C.—November 1, 5 p.m., *"Frederick William Hewitt,"* Frederick Hewitt Lecture by Dr. George Edwards.

Royal Eye Hospital, St. George's Circus, Southwark, London, S.E.—November 1, 4 p.m., *"Clinical Ophthalmology"* (Revision), by Mr. R. A. Burn and Mr. R. P. Crick; 5.30 p.m., *"Ophthalmic Neurology,"* by Mr. L. H. Savin.

Royal Institute of Public Health and Hygiene, 28, Portland Place, London, W.—November 1, 3.30 p.m., *"The Contribution of the Blind to the Community,"* by Mr. W. G. Askew.

Society of Public Analysts and Other Analytical Chemists.—At Chemical Society, Burlington House, Piccadilly, London, W., November 1, 7 p.m., *"Chemical Determination of Magnesium in Cast Iron,"* by Messrs. W. Westwood and R. Presser; *"The Determination of Sodium in Aluminium and its Alloys by Vacuum Distillation,"* by Messrs. W. McCamley, T. E. L. Scott, and R. Smart; *"The Determination of Lead Oxide in the Presence of Lead,"* by Mr. R. M. Black.

Thursday

British Postgraduate Medical Federation.—At London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C., November 2, 5.30 p.m., *"Tissue Defences in the Early Stages of Infection,"* by Dr. A. A. Miles.

Honyman Gillespie Lecture.—At University New Buildings (Anatomy Theatre), Teviot Place, Edinburgh, November 2, 5 p.m., *"The Place of Chemotherapy in the Treatment of Pulmonary Tuberculosis,"* by Dr. C. W. Clayson.

●Institute of Dermatology, Lisle Street, Leicester Square, London, W.C.—November 2, 5 p.m., *"Bullous Eruptions,"* by Dr. H. J. Wallace.

Institute of Psychiatry, Maudsley Hospital, Denmark Hill, London, S.E.—November 2, 3 p.m., *"The Nature of the Electroencephalogram,"* by Dr. Denis Hill.

Institute of Urology (University of London).—At St. Paul's Hospital, Henrietta Street, London, W.C., November 2, (1) 3 p.m., ward round by Mr. H. G. Hanley; (2) 5 p.m., *"Malignant Disease of the Prostate,"* by Mr. J. D. Fergusson.

London University.—At Royal Society of Medicine, 1, Wimpole Street, London, W., November 2, 5 p.m., *"The Development and the Present Use of Bronchospirometry,"* Semon Lecture by Dr. Paul Frenckner (Stockholm).

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—November 2, 5.30 p.m., "*Operative Surgery*," by Miss J. M. Dollar.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—November 2, 4.30 p.m., lecture-demonstration on neurology by Dr. A. Feiling.

Friday

LONDON UNIVERSITY.—At University College Hospital Medical School, University Street, London, W.C., November 3, 5 p.m., "*The Circulation in Pregnancy*," by Professor R. J. Kellar (Edinburgh).

●MAIDA VALE HOSPITAL MEDICAL SCHOOL, London, W.—November 3, 5 p.m., clinical neurological demonstration by Dr. Redvers Ironside.

●ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS, 58, Queen Anne Street, London, W.—November 3, 12 noon, "*Tumours in the Pouch of Douglas*," by Mr. R. B. K. Rickford; 3 p.m., "*Controversial Procedures in Obstetric Practice*," by Mr. D. Fyfe Anderson; 5 p.m., "*Any Questions?*" Mr. J. E. Stacy (chairman), Dr. G. Gordon Lennon, Dr. D. Fyfe Anderson, Mr. W. J. H. M. Beattie, and Mr. J. V. O'Sullivan.

●ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—November 3, 3.45 p.m., "*The Application of Biochemistry to Clinical Problems*," by Dr. N. Martin.

ROYAL MEDICAL SOCIETY, 7, Melbourne Place, Edinburgh.—November 3, 8 p.m., "*Headache*," dissertation by Mr. J. R. A. Harvey.

ROYAL SANITARY INSTITUTE.—At Council Chamber, Town Hall, Leicester, November 3, 10 a.m., Leicester Sessional Meeting. Papers: "*The Development of Main Drainage in Leicester*," by Mr. H. Bird, A.M.I.Mun.E.; "*Current Problems in Tuberculosis*," by Dr. J. Cuthbert.

Saturday

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, London, W.C.—November 4, 11 a.m., "*A New Form of Surgical Treatment for Ménière's Disease*," by Dr. Paul Frenckner.

●ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS, 58, Queen Anne Street, London, W.—November 4, 9.45 a.m., "*The Long First Stage*," by Dr. Gladys Hill; 11.30 a.m., "*Vaginal Hysterectomy*," by Dr. G. Gordon Lennon.

APPOINTMENTS

LIVERPOOL REGIONAL HOSPITAL BOARD.—The following senior medical staff appointments are announced: *Consultant Ophthalmologist to Sefton General Hospital*, D. A. Barton, M.B., Ch.B., D.O.M.S. *Consultant Otorhinolaryngologist to Children's Hospital, Birkenhead*, G. A. Moulden, M.B., Ch.B., D.L.O. *Whole-time Consultant Radiotherapist to Liverpool Radium Institute*, M. S. Milln, M.D., D.M.R.T. *Consultant Obstetrician and Gynaecologist to hospitals in Warrington*, G. Millington, M.B., Ch.B., M.R.C.O.G. *Whole-time Consultant Physician to Walton Hospital*, C. J. Williams, M.D., M.R.C.P. *Consultant Paediatrician to Hospitals in Warrington area*, H. Angelman, M.D., M.R.C.P., D.C.H. *Tuberculosis Medical Officer (whole-time) for South and Central Liverpool areas*, S. Keidan, M.B., Ch.B., C.P.H. *Assistant Ophthalmologist to Bootle General Hospital*, D. Black, M.B., Ch.B., B.A.O., D.O.M.S. *Assistant Radiologist (whole-time) for North Liverpool area*, J. Winter, M.B., Ch.B., D.M.R.D., M.Rad. *Assistant Radiologist (whole-time) to Warrington and St. Helens areas*, A. M. Frazer, M.R.C.S., L.R.C.P., D.M.R.D., M.Rad.

O'BRIEN, GERALD, M.B., Ch.B., D.P.H., Medical Officer of Health and School Medical Officer, County Borough of St. Helens.

WALLACE, E. J. GORDON, M.B., Ch.B., D.P.H., Medical Officer of Health, Portland, Dorset. (In addition to appointments already held.)

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Lewis.—On October 9, 1950, to Evelyn R. Lewis, M.B., Ch.B., wife of Charles L. Lewis, M.B., Ch.B., D.M.R.T., a daughter.

Mansour.—On October 12, 1950, at Liverpool Maternity Hospital, to Enid Eileen (formerly Huston), wife of Dr. Joseph Mansour, a daughter.

Webster.—On October 13, 1950, at the Central Middlesex Hospital, London, N.W., to Jean M. Webster (formerly Gilbert), M.B., B.S., wife of Mr. T. J. Webster, B.Sc., A.R.I.C., a daughter—Clare.

Wright.—On September 29, 1950, at Lincoln, to Margaret, wife of Dr. Trevor Wright, a daughter.

DEATHS

Bainbridge.—On October 10, 1950, at Sedbro House, Brough, Westmorland, Isaac Bainbridge, M.D.

Caird.—On October 12, 1950, at 25 Musters Road, West Bridgford, Nottingham, Karl Francis Caird, M.B., F.R.C.S.Ed.

Davison.—On October 11, 1950, at 1, Arthington Avenue, Harrogate, Robert Collinson Davison, M.B., B.S.

Foggo.—On October 6, 1950, at Pinelands, Capetown, South Africa, Cecil Gordon Foggo, L.R.C.P.&S.Ed., aged 82.

Goldmann.—On October 17, 1950, Arthur Goldmann, M.D., of London, N.W., aged 77.

Greig.—On October 18, 1950, at Kensington, London, Janet Lindsay Greig, M.B., of Melbourne, Australia.

Liston.—On October 18, 1950, at Garramore, Morar, Inverness-shire, William Glen Liston, C.I.E., M.D., F.R.C.P.Ed., F.R.S.Ed., Lieutenant-Colonel, I.M.S., retired, aged 78.

Newman.—On October 15, 1950, at his home, 34, Eagle Lane, Snaresbrook, London, E., Edmund James Newman, M.R.C.S., L.R.C.P.

Robertson.—On October 14, 1950, at Kenilworth Lodge, Clarendon Road, Southsea, Hants, Claude Robertson, M.B., Ch.B.

Wolfsohn.—On October 2, 1950, at Hampstead General Hospital, Else Wolfsohn, L.R.C.P.&S.Ed., L.R.F.P.S.Glas., of 49, Belsize Park Gardens, London, N.W.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Vaccination

Q.—*My daughter, who is 2 years old, has not been vaccinated. If she is done now, is she likely to have a more severe reaction than, say, at 6 months of age?*

A.—While primary vaccination is usually recommended at the age of 4 to 6 months, when any passive immunity derived from the mother will have disappeared, there is no likelihood that a child vaccinated at the age of 2 years will have a more severe reaction than would have occurred at 6 months. The multiple pressure technique should be used. In many countries primary vaccination is done just before school entry. The very small risk of post-vaccinal encephalitis occurs mostly with school-children and adolescents.

Immunization and Poliomyelitis

Q.—*Is there any evidence that T.A.F. immunizing agent is less likely to precipitate paralysis in a child suffering from a subclinical attack of poliomyelitis than A.P.T.?*

A.—There is probably no evidence that immunization with T.A.F. is less likely to be followed by paralysis than is the case with A.P.T., since T.A.F. is not used on any large scale for the immunization of young children. The data produced in this country and in Australia indicate that the combined diphtheria-pertussis vaccine and A.P.T., both of them alum-containing reagents, have been associated with paralysis in poliomyelitis, whereas in Canada, where formol toxoid (F.T.) only is used, no evidence of this phenomenon has so far been found. It is only fair to say, however, that in many areas in Britain no association between poliomyelitis and injections of A.P.T. has been detected by analysis of immunization records. On the other hand, paralysis following inoculation of other reagents, such as penicillin, has occasionally been reported, although it is difficult to say what significance to attach to these rare happenings.

The medical officer of health in any area must decide in what circumstances he should cease immunization against diphtheria, or modify the procedure, in order to avoid any added risk of paralytic poliomyelitis. Such expedients as avoiding intramuscular injections, immunizing only infants under 1 year of age, and the use of F.T. or T.A.F. have all been recommended. As an alternative to A.P.T. for large-scale immunization, F.T. would probably be preferable to T.A.F., but, again, three instead of two inoculations are required. This procedure should not create any administrative difficulties where children are being inoculated at child-welfare clinics.

Teething

Q.—*Can any infant ailments, beyond local reaction, be justly ascribed to "teething"?*

A.—Teething may be a physiological process, but, as the late Sir Frederic Still used to remark, so is labour, and yet it may be painful and associated with various disorders. The pain of teething may lead to restlessness and sleeplessness, and possibly, in the child otherwise predisposed—potentially epileptic (?); rickety, with low blood calcium (?)—to convulsions. The "local reaction" resulting in a stomatitis may spread and result in a pharyngitis, otitis media, cervical adenitis, bronchitis, and even pneumonia. Absorption of toxins may result in a parenteral "diarrhoea and vomiting" disturbance. A rash of the lichen urticaria type may be attributed to the same cause. The pain and tenderness also produce a dislike for food and therefore to loss of appetite and weight. The healthy baby is much less likely to be upset by teething than the weakly infant, and it is difficult therefore to sort out which ailments are directly

attributable to teething and which are due to associated conditions at the teething age when feeding changes are in progress. Sore buttocks, for example, may occur at this time, and it is almost impossible to say whether this can be "justly ascribed" to teething or not.

The Vegetable Marrow

Q.—*My wife and I have independently noticed that our nights have been disturbed after eating vegetable marrow for supper. Is marrow known to contain a diuretic principle?*

A.—While there is no reference to the vegetable marrow, *Cucurbita ovifera*, as containing a diuretic principle, other members of the *Cucurbitaceae* are said to contain one. The white gourd melon and the bottle gourd are diuretic according to K. M. Nadkarni's *Indian Materia Medica* (Bombay, 1927), and the *United States Dispensatory* (1943) says that bottle gourd is a native remedy for dropsy in the Sandwich Islands.

Vesical Calculus

Q.—*A male patient has recurrent attacks of backache, sometimes radiating to the legs. X-ray shows a stone, the size of a lentil, at the neck of the bladder. Is surgical removal of the stone advised?*

A.—It appears probable that the pain is due to the calculus impacted at the vesical neck. There should be no difficulty about removing it by perurethral methods through a cystourethroscope; it can either be withdrawn or pushed back into the bladder and crushed. These are surgical measures, of course, but it is unlikely that without some such treatment the stone can be got rid of, although there is always a chance of spontaneous expulsion. It certainly should not be left where it is, otherwise a whole host of troubles, such as chronic prostatitis, which may be very serious, are likely to result.

Dangers of Detergents

Q.—(*a*) *Have modern detergents any tendency to produce dermatitis of the hands?* (*b*) *Are they harmful to the bacterial flora of a domestic septic tank?* (*c*) *Do they help prevent the soakaway pit of a domestic sewage disposal system from "greasing up"?*

A.—(*a*) Most modern detergents even when used in the strength recommended by the makers are alkaline, though less so than soaps and household powders. They are therefore capable of producing a traumatic dermatitis as a result of damage to the natural fatty and keratin protection of the skin surface. This may be avoided by the subsequent use of emollients. Dermatitis from specific sensitization may arise, but is rare.

(*b*) The use of detergents has created new problems in sewage purification. Research on this subject is at present going on in various parts of the country, but the results are as yet inconclusive. This is to some extent because detergents vary quite widely in their composition, and conclusions which are valid for one do not necessarily apply to the others. The results so far obtained by experiment would seem to show that detergents are not deleterious to a sewage purification plant in the quantities at present used, and it is probable that this conclusion applies also to domestic septic tanks.

(*c*) The tendency of detergents will be to prevent the greasing up of the soakaway pit, but we doubt if the quantities normally used will in practice make any appreciable difference.

"Gammexane"

Q.—*What are the symptoms and signs of "gammexane" poisoning? Is it possible that effects noticed after the use of crude commercial powder, which contains impurities with a markedly unpleasant smell, are due to these impurities?*

A.—Gammexane is the trade name for a preparation containing as its main ingredient the gamma isomer of hexachlorcyclo-hexane, sometimes called benzene hexachloride.

There are no reports of accidental poisoning in man, so that the symptoms to be described are those found in experimental animals. Cameron and Burgess (unpublished) describe the following symptoms in guinea-pigs and rabbits after a single poisonous dose given by mouth: "Increased respiration, restlessness, increased micturition, intermittent spasms, salivation, grinding of the teeth, backward movements, loss of balance, head retraction, and convulsions (at first intermittent and then sustained with limbs outstretched), ending in collapse and death. In large single doses the gamma isomer causes death from functional disturbance of the central nervous system, especially of the respiratory centre, and this often results in cardiac failure and lung oedema." In chronic poisoning the animals exhibit constant muscular tremors culminating in convulsions of increasing severity until death. The fur of white rats often becomes markedly discoloured. There are no striking pathological changes in chronically poisoned animals.

The question mentions "effects" (presumably on man), but does not state their nature. The impurities in the commercial preparations are responsible for the smell and also for the unpleasant taint given to food by some preparations of hexachlor-cyclo-hexane. In experimental animals the symptoms produced by feeding commercial preparations or a mixture of the pure isomers are similar, so that there is no reason for supposing that these impurities have any special toxic properties.

NOTES AND COMMENTS

Thrombophlebitis Migrans.—Dr. John Gibbens (London) writes: As a postscript to your answer to the question on thrombophlebitis migrans in "Any Questions?" (October 14, p. 901), I think your questioner ought to be told that this disease is often associated with carcinoma. I have personally seen three such cases, the first two associated with carcinoma of the stomach, the third with carcinoma of the head of the pancreas. The first case was unsuspected during life, and it was only when a second case also proved to have carcinoma of the stomach that I made a search through the literature, to find that there are plenty of cases reported with this curious association. With the third case I guessed that the patient had carcinoma, but *x* rays of the stomach showed nothing, though there could be no doubt about the malignant cachexia. The carcinoma was discovered post mortem. After this experience I should certainly be in favour of a thorough investigation for latent carcinoma.

Corrections

In the item of "Medical News" entitled "Visitor to Copenhagen" (October 21, p. 956) we stated that the anaesthesiology centre in Copenhagen has until now been in charge of anaesthetists from the U.S.A. This was incorrect, for in fact Dr. T. C. Gray, of Liverpool, is at the centre now, and will remain in Copenhagen for two months.

Dr. C. C. Ungley (Newcastle-upon-Tyne) writes: Your excellent leading article (October 21, p. 933) on the absorption of vitamin B_{12} is incorrect in one particular. It is true that Ternberg and Eakin (*J. Amer. chem. Soc.*, 1949, **71**, 3858) showed that a constituent of normal gastric juice combines with vitamin B_{12} to render it microbiologically unavailable, and that Cuthbertson and I have confirmed this. On the other hand, we have not assumed—neither did Ternberg and Eakin—that the vitamin B_{12}-combining factor was identical with Castle's intrinsic factor. Indeed there is already some evidence to the contrary (Prusoff, *Amer. Chem. Soc.*, 1950, 118th meeting). I entirely agree that caution is needed in interpreting complex therapeutic experiments. I have already mentioned some of the difficulties involved in judging the absorption of vitamin B_{12} from the oral-dose/parenteral-dose ratio. An additional difficulty is the variable excretion of vitamin B_{12} in the urine, which is likely to be greater after parenteral than after oral administration.

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